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CONTENTS

Page

Page

ORIGINAL ARTICLES

- Intravenous Saline.** *By G. E. Dunkerley, M.B., B.S. (Lond.), F.R.C.S. (Edin.)* .. 3

- Squamous Metaplasia and Keratinization in Cystic Hyperplasia of the Human Breast.** *By C. Mohan Rangam, M.D.* 9

- Pulmonary Moniliasis.** *By Khushdeva Singh, M.B., B.S., F.C.C.P., T.D.D., Major* 10

- Contra-lateral Fracture of the First Rib following Thoracoplasty.** *By H. B. Dingley, M.B., B.S., T.D.D.* .. 14

- Oral Novocaine Therapy in Peptic Ulcer.**
A study of 20 cases. *By T. Thomas and M. V. Kamath* 16

- Cup Arthroplasty in Hip Joint Surgery.**
By M. G. Kini, M.B., M.Ch. (Orth.), F.R.C.S. (Edin.), F.A.C.S., F.R.S. (Edin.), F.N.I., F.A.Sc., F.I.C.S., and I. Chalapathy Naidu, M.B., M.S. .. 19

A MIRROR OF HOSPITAL PRACTICE

- Sexual Disorder in 'Mepacrine Psychoses'.** *By K. B. Kapur, M.B., B.S., and P. R. Das Gupta, D.T.M.* .. 20

OCCASIONAL NOTES

- The Venereal Disease Programme of the World Health Organization. The Simla training centre and demonstration area.**
Presentation by John C. Cutler, M.D. .. 22

EDITORIAL

- The Birth of the Indian Republic** .. 25

MEDICAL NEWS

- BRITISH EXPEDITION'S SEARCH FOR MEDICINAL PLANT** 25
- PROGRESS TOWARDS AN INTERNATIONAL PHARMACOPŒIA** 26
- VAUXHALL REHABILITATION CENTRE** .. 27
- MATERNAL AND CHILD HEALTH** .. 27
- AMENDMENTS TO DRUG RULES, 1945** .. 28
- INTERNATIONAL HONOUR FOR INDIAN SCIENTIST : DR. ZAL R. KOTHAVALA** .. 28
- THE DR. B. S. SHROFF MEMORIAL GOLD MEDAL OF THE BOMBAY MEDICAL UNION, 1949** 28

(Continued on page 2)

CONTENTS—(Continued from page 1)

	Page		Page
THE DR. SIR BHALCHANDRA KRISHNA, Kt., MEMORIAL GOLD MEDAL OF THE BOMBAY MEDICAL UNION, 1949	29	REVIEWS	
FIFTY YEARS AGO		SKIN DISEASES IN GENERAL PRACTICE. By F. Ray Bettley, T.D., M.D., F.R.C.P. 1949	32
THE CALCUTTA HEALTH OFFICER'S REPORT (<i>Indian Medical Gazette</i> , 1900, Vol. 35; p. 29)	29	A SYNOPSIS OF OBSTETRICS AND GYNÆ- COLOGY. By Aleck W. Bourne, M.A., M.B., B.Ch., F.R.C.S. Tenth Edition	32
CURRENT TOPICS, ETC.		DISEASES OF WOMEN. By Ten Teachers, C. White, F. Cook, Sir William Gilliatt and others. Eighth Edition ..	32
NEW TOOL FOR THE KITCHEN (<i>Medical Press</i> , Vol. 221, 16th March, 1949, p. 261)	30	PRINCIPLES OF HUMAN PHYSIOLOGY (STARLING). By C. Lovatt Evans, D.Sc., F.R.C.P., F.R.S., LL.D. Tenth Edition	33
FOLIC ACID INCOMPATIBILITIES (<i>Pharma- ceutical Journal</i> , Vol. 162, 18th June, 1949, p. 458)	30	BOOKS RECEIVED ..	33
TRAVEL SICKNESS (<i>Medical Review</i> , Vol. 43, June 1949, p. 81)	30	ABSTRACTS FROM REPORTS	
ORAL REACTIONS TO PENICILLIN. By W. G. Cross (<i>Brit. Med. Jour.</i> , i, 29th January, 1949, p. 171), as abstracted in the <i>Acta Medica Orientalia</i> , Vol. 8, January- February 1949, p. 31)	31	ANNUAL REPORT OF THE CHEMICAL EXAMINER'S DEPARTMENT FOR THE YEAR 1948. PRINTED BY THE SUPERINTENDENT, GOVERNMENT PRESS, MADRAS. 1949 ..	33
THE EXCRETION OF PENICILLIN IN HUMAN MILK. By R. Rozansky and A. Brzezinsky (<i>Journal of Laboratory and Clinical Medicine</i> , Vol. 34, April 1949, p. 497)	31	CORRESPONDENCE	
THE PROBLEM OF WEAKNESS AND FATIGUE. By M. Y. Silver (<i>American Practitioner</i> , Vol. 3, June 1949, p. 598)	31	TREATMENT OF MALARIA	33
		TYPHUS IN THE NORTHERN CIRCARS ..	33
		MEDICAL CORRESPONDENCE COLLEGE ..	34
		COMBINATION OF LIVER EXTRACT AND FOLIC ACID	34

Original Articles

INTRAVENOUS SALINE

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F.R.C.S. (Edin.)

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THE administration of fluids by intravenous drip is recognized as an indispensable adjunct to the treatment of many conditions. So much is this accepted as a commonplace that there is a tendency to give large quantities of normal saline empirically, and without a critical consideration of the probable separate requirements of salt and water in the individual patient.

Normal saline is isotonic with the blood, and it was at first thought that the giving of normal saline intravenously 'was an easy and effective means of increasing blood volume' (Martindale, 1941). This supposition was invalidated by the physiological fact that intravenous normal saline only increases blood volume momentarily as there is a constant interchange of water and salt between the blood plasma (3 litres) and the tissue fluids (11 litres). Only custom has perpetuated its use. If water and salt were always excreted in the same proportion, and that in the proportion of salt to water which exists in normal saline, it would be logical to administer intravenous fluids in this strength, but this is not so. Of various excretions and secretions from the body only liquid motions and urine may average as much salt as is in normal saline. The chloride concentration in vomit or gastric aspirate, sweat, bile and intestinal fluid is about that of $\frac{1}{2}$ N saline and the moisture in expired air does not contain salt. Intravenous salt and water should be given then, not to raise the blood volume, but to replace a deficiency in salt and water in the body fluids.

It is suggested that good grounds exist for a more careful approach to the problem of determining a patient's requirements. Attention is once more drawn to the often repeated fact that if relatively too much salt is given the patient will continue to suffer from thirst, and that despite the absence of clinical signs of dehydration, even in the presence of oedema, there may actually be cellular dehydration. Relative hypertonicity of tissue fluids gives rise to a tendency for fluid to be conveyed out of the cells by osmosis. These facts and the details of metabolism of water and salt have been authoritatively dealt with by Marriott (1947). If too little salt is given dehydration may not be overcome as hypotonic solutions provoke diuresis.

The occurrence of oedema in patients given continuous drip intravenous normal saline for several days prompted this clinical investigation. The following physiological and clinical facts were first considered:—

Water requirements

The normal daily intake of water is:—

- (1) Fluid drunk = 1,000–2,000 cc./day.
- (2) Food = 1,000–2,000 cc./day.

The lowest adequate daily intake is thus about 2,000 cc. This intake is balanced by a loss of water:—

- (1) Skin and breath = 800–4,000 cc./day.

The latter figure is only reached in hot climates and under strenuous conditions.

- (2) Urine = 500–1,500 cc./day.

The kidneys usually excrete 35 g. solids daily. At least 500 cc. water is needed to prevent retention of part of this. If the kidneys are damaged they cannot concentrate the urine to the same degree, and if there is more solid to be excreted than usual more water is needed to dissolve it. To ensure lack of retention of substances which ought to be excreted in the urine therefore a patient's intake is so regulated as to provoke excretion of 1,000–1,500 cc. urine per day.

- (3) Faeces = 150 cc./day.

- (4) Vomit, fistula, sinus, alimentary aspiration, diarrhoea.

The quantity in each case must be taken into account.

It follows that a patient excretes from 2,000 to 6,000 cc. of fluid daily and of course a normal excretion of water of at least 2,000 cc. demands an intake of a corresponding amount.

Sodium chloride requirements

The normal daily intake of salt is 5 to 10 g. and it is all gained from food or from certain beverages, e.g. beer. Salt is lost by urine, faeces, sweating, lactation, vomiting and in less amounts by other processes. The level of salt in the urine usually corresponds to about N saline, i.e. approx. 9 g./litre. (The maximum possible is 2 per cent or 20 g./litre.) Salt concentration in sweat may reach the level of $\frac{1}{2}$ N saline but is never more and generally much less. Under abnormal conditions salt may be lost in gastric aspirate, vomit, watery motions or fistulae. Gastric aspirate or vomited material usually contains an amount of salt corresponding to that in $\frac{1}{2}$ normal saline, but under normal conditions nearly all salt loss is *via* the kidneys.

Water and salt deficiency

Clinical signs of lack of water are thirst, oliguria, high-coloured urine, sunken eyes, pinched features, dry inelastic skin, dry tongue and, in infants, receding fontanelles. Clinical

dehydration is discernible when 6 per cent of the body weight has been lost. Example: Body weight = 70 kg. 6 per cent = 4.2 kg. = 4 litres approx. This means that a clinically dehydrated 11-stone man requires 4 litres of water to make up the amount by which his body fluids have been depleted. Such a patient will also need 2 litres for his daily requirement. To bring his body fluids up to normal within 24 hours the patient will therefore require 6 litres of water (apart from salt requirements). On subsequent days he will need 2 litres of water a day in some form. It is not essential to make up the whole of a patient's water deficiency in 24 hours and it would be quite logical to give 4 litres on each of the two first 24-hour periods and then 2 litres per day. If this amount of fluid were administered intravenously in the form of normal saline it is clear that the patient would receive 36 g. on each of the first two days and 18 g. on subsequent days. Even if the urine contained the abnormally high figure of 20 g./litre the secretion of 1,800 cc. of urine daily would be necessary to rid the body of all excess salt during the first two days, and 3,600 cc. of urine daily if the urine contained a normal amount of 9 g./litre. As the individual under consideration is dehydrated with a fluid intake of 4 litres intravenously it is obvious that nothing like 3,600 cc. would be available for urinary secretion. In other words salt retention would be likely. Physiological considerations thus indicate that patients receiving normal saline for several days eventually become oedematous (from salt retention) and yet may die of lack of water (cellular dehydration). This has been observed as a matter of practical experience.

If salt intake is diminished or excess of salt is lost alkalosis occurs especially if renal disease be present. The symptoms are headache, nausea, vomiting, drowsiness and coma. Tetany may follow. Salt deficiency may also lead to cramp-like muscular pain.

To calculate the amount of salt required with a large amount of intravenous water the patient's plasma chloride and weight must be measured. Then 0.5 g. sodium chloride per kilo body weight is administered for every 100 mg. by which the plasma chloride is to be raised.

Example.—Body weight = 70 kg. Plasma chloride = 510 mg./100 cc. Salt required = $0.5 \times 0.5 \times 70 = 17.5$ g. or about the equivalent of 2 litres of N saline.

A patient with a plasma chloride of 510 mg. is usually clinically dehydrated. His water requirement in the first 24 hours would be at least 4 litres. To administer 4 litres of water and 17 g. of salt together the strength of the solution must be $\frac{1}{2}$ normal saline.

Further in a normal patient the daily requirement of salt is only 5 to 10 g. (the quantity contained in 500 to 1,000 cc. N saline). No doubt the requirement in an oliguric patient is less. It thus appears that if 500 cc. of N saline were given every 24 hours, together with an additional 500 cc. to compensate for possible excessive salt loss (e.g. sweating in operation theatre), i.e. in all 1,000 cc., an adequate daily amount of salt would be administered. As the fluid requirement is at least 2,000 cc. for 24 hours, it is clear that $\frac{1}{2}$ N saline is the best form in which to provide a patient's salt and water needs when alimentary administration is impossible. The addition of 5 per cent glucose is advantageous. This observation that a hypotonic solution is desirable for administering water and salt intravenously has been made on numerous occasions previously and has been recommended for children, for the Army in India, and by Edwards (1948). Salt is found in the following concentrations in body excreta and secretions:

Sweat—less than 5 g./litre.

Vomit—3.3 g./litre (Edwards, 1948).

Urine—9.25 g./litre (average of 12 early morning specimens from patients with trivial injuries in cool weather in India). 7 g./litre (average of 24 specimens from patients receiving $\frac{1}{2}$ N 5 per cent glucose saline). 6 g./litre (Wright, 1938).

Gastro-duodenal aspirate 5.7 g./litre (Edwards, 1948).

It follows that replacement demands the giving of hypotonic salt solution. Edwards (1948) recommends administering fluids to those suffering from water depletion in the form of a saline solution containing 0.16 per cent NaCl

Name	Occupation	Mine	Date of admission	
24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Clinical dehydration	Signs of oedema
			Plasma chloride mg./100 cc.	Urine chloride g./litre
			Urine volume (cc.)	Intravenous water (litres)
			Intravenous salt (grammes)	How given
				Remarks

and 5 per cent dextrose or glucose. Losses of salt, he suggests, should be made up by giving normal saline. In the Royal Infirmary, Edinburgh, in 1947, two fluids were in common use: (a) N saline, and (b) distilled water.

From a consideration of all the foregoing and in the hope of simplifying the work of medical officers, nursing staff and dispensers by producing a single solution suitable for all cases requiring intravenous fluid (apart from those requiring plasma or blood), it was decided to use $\frac{1}{2}$ N 5 per cent glucose saline and to study the results. This simplification would lessen mistakes and was considered highly desirable if consistent with satisfactory results.

The above proforma was used in the cases studied.

Examples of plasma chloride estimations by Whitehorn's method were:—

Case number	Day of intravenous therapy	Mg./100 cc. plasma
11	6	618
14	4	606
15	1	518
26	2	665

Urinary chloride was estimated by Fantus test (Marriott, 1947), using the early morning specimen. It was soon realized that provided the urinary chloride and volume were known a knowledge of the plasma chloride was unnecessary. Furthermore, plasma chlorides estimated in a patient receiving saline intravenously may be fallacious. In addition the utmost simplification was aimed at and therefore plasma chlorides were seldom estimated.

Conditions for which intravenous fluids had to be given in the K. G. F. Hospital from April to December 1948. (Some cases without full records were excluded.)

Lobar pneumonia	8
Partial gastrectomy for duodenal ulcer ..	5
Cholera (bacteriologically proved) ..	4
Perforated duodenal ulcer	4
Acute gastro-enteritis	3
Perforated appendix	2
Right hemicolectomy for tuberculosis ..	2
Meningococcal meningitis	1
Gastro-jejunostomy for pyloric obstruction	1
Bacillary dysentery	1
Incarcerated inguinal hernia	1
Strangulated hernia	1
Ruptured left tubal pregnancy	1
Amputation left leg for moist gangrene ..	1
Extensive burns	1
TOTAL ..	36

Illustrative case records

A. Lobar pneumonia. It was customary in the period during which these observations were made (1948) to treat cases of pneumonia with sulpha drugs. In cases of vomiting, delayed response, inability to take or absorb tablets, hæmaturia, etc., intravenous $\frac{1}{2}$ N 5 per cent glucose saline was given and treatment continued with soluble sulphadiazine intravenously.

Case 1.—Admitted on 14th April, 1948. Temperature normal on 24th April, 1948. Out-patient on 7th May, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
17-4-1948	1,740	3,802	3	1,080	3
18-4-1948	1,350	855	4	750	3
19-4-1948	330	150	3	750	3

There was no response to soluble sulphadiazine and treatment was discontinued and intravenous saline stopped. It will be noted that the adverse gastric balance of 2,062 cc. was not offset by a sufficiently high intravenous quota on 18th and that in consequence urine secretion was only 750 cc. despite the retention by mouth of 495 cc. of fluid.

Case 8.—Admitted on 14th October, 1948. Afebrile on 19th October, 1948. Out-patient on 27th October, 1948. Was dehydrated on admission and had vomited many times.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
15-10-1948	240	330	N.R.	Nil	3
16-10-1948	1,200	Nil	5	1,200	3
17-10-1948	1,950	150	8	1,080	4
18-10-1948	2,310	Nil	3	1,440	3
19-10-1948	2,970	Nil	N.R.	1,440	Nil

There was reason in these pneumonia cases for the parenteral administration of intravenous sterile distilled water instead of saline, as the main rationale of administration was to avoid all likelihood of sulpha drug crystalluria, hæmaturia or anuria, by provoking a diuresis. However, as the records show, the solution used, $\frac{1}{2}$ N 5 per cent glucose saline, gave rise to a satisfactory diuresis and did not provoke the slightest tendency to chloride retention as is shown by the urinary chloride levels.

B. Meningococcal meningitis in a child aged 4.

Case 9.—Admitted on 14th May, 1948. Afebrile on 21st May, 1948. Out-patient on 16th June, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
15-5-1948	N.R.	N.R.	N.R.	N.R.	2
16-5-1948	600	Nil	5	900	1½
17-5-1948	N.R.	N.R.	4	750	1
18-5-1948	N.R.	N.R.	6	1,500	1
19-5-1948	N.R.	N.R.	4	1,560	0

C. Partial gastrectomy for duodenal ulcer.

Case 11.—Operation on 25th August, 1948. Out-patient on 27th September, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
26-8-1948	Nil	465	5	660	3
27-8-1948	15	1,080	5	1,950	3
28-8-1948	22	1,335	7	1,530	2
29-8-1948	360	1,680	9	1,890	2
30-8-1948	270	1,365	11	1,200	2½
31-8-1948	990	930	3	N.R.	Nil

Case 12.—Operation on 31st September, 1948. Out-patient on 1st November, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
1-9-1948	Nil	120	3	900	4
2-9-1948	30	1,020	6	2,910	3
3-9-1948	210	1,545	N.R.	2,070	2
4-9-1948	465	1,245	5	1,020	2
5-9-1948	3,400	710	7	2,040	2

From a consideration of these cases it will be seen that the urine chloride remained at normal levels and that diuresis was maintained at a satisfactory rate even in patients with an adverse gastric balance.

D. Case 15.—This man had gastro-jejunostomy for complete pyloric obstruction. The saline chart shows his records both before and after operation.

Date of admission 21st June, 1948. Date of operation 7th July, 1948. Out-patient on 5th August, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
22-6-1948	60	1,590	3	30	4
23-6-1948	Nil	Nil	5	2,880	5
24-6-1948	510	Nil	5	3,000	5
25-6-1948	930	Nil	9	1,590	2
26-6-1948	1,020	Nil	5	2,070	2
27-6-1948	1,800	Nil	6	1,260	Nil
28-6-1948	2,130	Nil	Not recorded.	1,500	Nil
7-7-1948	1,020	120	Not recorded.	1,350	2
8-7-1948	Nil	Nil	11	600	3
9-7-1948	1,440	180	4	1,440	2
10-7-1948	990	15	7	2,400	2

The good gastric intake before operation was achieved by small feeds every $\frac{1}{2}$ hour.

E. Case 17.—Right hemicolectomy for ilco-cæcal tuberculosis. Admitted on 17th September, 1948. Operation on 8th October, 1948. Out-patient on 3rd December, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
8-10-1948	Nil	Nil	6	480	4
9-10-1948	90	1,140	5	1,515	3
10-10-1948	930	Nil	11	750	Nil

Case 17 passed 480 cc. urine in the 24 hours after operation despite 4 litres of $\frac{1}{2}$ N 5 per cent glucose saline intravenously. Without parenteral therapy anuria would certainly have persisted for 2 to 3 days.

F. The next cases had general peritonitis from a perforated viscus.

Case 18.—Perforated duodenal ulcer on 18th May, 1948. Out-patient on 22nd June, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
19-5-1948	90	Nil	6	2,040	6
20-5-1948	Nil	Nil	9	780	4
21-5-1948	1,380	4,200	12	1,110	3
22-5-1948	2,820	2,970	12	1,440	3
23-5-1948	2,535	2,100	N.R.	1,620	..

Case 20.—Perforated duodenal ulcer on 27th September, 1948. Out-patient on 15th October, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
28-9-1948	<i>Nil</i>	90	8	840	4
29-9-1948	150	330	8	1,530	3
30-9-1948	960	2,055	10	1,440	3
1-10-1948	935	1,170	7	1,440	3

The urine volume was kept at the optimum level in this case.

G. The following cases were bacteriologically proved cholera. They needed remarkably large quantities of intravenous fluids. Despite these quantities their urinary chlorides remained normal.

Case 25.—Admitted on 17th September, 1948. Out-patient on 10th October, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
18-9-1948	<i>Nil</i>	2,040	..	<i>Nil</i>	7
19-9-1948	210	1,280	2	300	10
20-9-1948	1,500	<i>Nil</i>	7	570	4
21-9-1948	1,830	<i>Nil</i>	6	1,560	3
22-9-1948	2,220	<i>Nil</i>	7	1,350	<i>Nil</i>

The volume of the stools was not measured but would have been useful for estimating the amount of fluid needed intravenously. The chloride content of the motion was unfortunately not estimated either. It can be seen from the above that the urine secretion in 72 hours was less than a litre despite the intravenous administration of 21 litres of $\frac{1}{2}$ N 5 per cent glucose saline.

Case 26.—Admitted on 5th September, 1948. Died on 20th September, 1948. He was extremely ill but improved and then succumbed to cholera, typhoid and pneumonia.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
6-9-1948	870	1,020	N.R.	N.R.	18
7-9-1948	1,680	180	3	810	6
8-9-1948	2,100	<i>Nil</i>	5	600	7
9-9-1948	4,350	60	5	1,200	<i>Nil</i>

It was felt during the treatment of this case that the use of a stronger solution would have been advantageous because by rapid intravenous administration hydration of the tissues was easily restored only to recur with all its severity when the intravenous drip was slowed. It seemed that the hypotonic solution caused diuresis. The decision as to the usefulness of $\frac{1}{2}$ N glucose saline in cholera really depends on the chloride content of the motion which unfortunately was not tested. If it approached N saline then the correct method of intravenous fluid replacement would be by N saline. However, it is probable that $\frac{1}{2}$ N saline is adequate and that it is but the nature of the disease which results in recurring attacks of dehydration. The urine chlorides were maintained at satisfactory levels and in case 26 the plasma chloride recorded on 7th September, 1948, was 685 mg./100 cc. Moreover, the urinary volume was moderate in most instances.

H. Case 33.—Admitted on 16th July, 1948, with strangulated hernia necessitating resection. Out-patient on 7th August, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
17-7-1948	<i>Nil</i>	<i>Nil</i>	N.R.	<i>Nil</i>	2
18-7-1948	990	2,055	5	630	4
19-7-1948	1,920	3,060	3	360	1
20-7-1948	1,860	330	4	1,290	<i>Nil</i>

Case 34.—Admitted on 3rd September, 1948, with intra-peritoneal hæmorrhage from ruptured left tubal pregnancy. Out-patient on 4th October, 1948.

24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine chloride (g./litres)	Urine volume (cc.)	I.V. $\frac{1}{2}$ N 5 per cent glucose saline (litres)
4-9-1948	<i>Nil</i>	<i>Nil</i>	N.R.	<i>Nil</i>	3
5-9-1948	4,050	N.R.	4	1,700	3
6-9-1948	780	1,005	6	1,920	2
7-9-1948	2,190	480	5	1,890	3
8-9-1948	3,360	<i>Nil</i>	N.R.	730	<i>Nil</i>

This patient's hæmoglobin percentage (Sahli) was 28 before operation and only one pint of blood was available and was given during operation. No blood or plasma was subsequently available and as vomiting was troublesome for days she had $\frac{1}{2}$ N 5 per cent glucose saline.

Discussion

As the case records detailed above show that the administration of $\frac{1}{2}$ N 5 per cent glucose

saline always resulted in a satisfactory balance as portrayed by the urinary chloride and urinary excretion figures it is now suggested that the only essential information needed is urinary output. An estimate of the quantity of $\frac{1}{2}$ N 5 per cent glucose saline required in the next 24 hours is made from a consideration of the urinary output in the previous 24 hours. Of course in an acutely ill patient the periods under consideration need not necessarily be so long as a day and the position can be reviewed every 6 or 8 hours but on the whole a daily estimate has been found adequate.

The optimum excretion of 1,500 cc. of urine can be secured by a fluid intake of 2 to $2\frac{1}{2}$ litres, and with variations of urinary output the proposed intake may be altered accordingly thus :

Urinary output in previous 24 hours (cc.)	Intravenous $\frac{1}{2}$ N glucose saline required in next 24 hours (litres)
Nil	4
500	$3\frac{1}{2}$
1,000	3
1,500	$2\frac{1}{2}$
2,000	2
2,500	$1\frac{1}{2}$
3,000	1

The proforma proposed now is simplified thus :

Name	Occupation	Mine	Date of admission		
24-hour period ending at 7 a.m. on	Gastric intake (cc.)	Gastric output (cc.)	Urine volume (cc.)	Intravenous $\frac{1}{2}$ N 5 per cent glucose saline (litres)	REMARKS

When $\frac{1}{2}$ N 5 per cent glucose saline was given intravenously patients suffered neither from salt depletion nor excess. As will be seen the urine chloride varied between limits of about 2 and 16 g./litres but was never absent, indicating serious salt depletion, nor stayed at a high figure for more than one daily estimation.

For this reason it can justifiably be concluded that the laboratory testing of urinary chloride is unnecessary. Provided the solution $\frac{1}{2}$ N 5 per cent glucose saline is used only the quantity for the next 24 hours need be calculated. This can be done during the morning round from a consideration of the previous day's urinary output. Usually an excess of intake over output of about $2\frac{1}{2}$ litres gives rise to a urinary excretion of 1,500 cc. and this is the quantity

aimed at. Should urinary excretion fall to nil at least 4 litres are required, but if urinary excretion is very high, e.g. 3,000, the solution, if given at all, should be in a quantity of only about 1 litre. Additional objections to the routine use of urinary chloride estimations are (a) patients needing intravenous therapy are often anuric or oliguric and urine may not be obtained for hours after treatment has begun; (b) urinary chloride level is affected by the quantity of salt given intravenously and the speed at which it is given.

The administration of sodium chloride intravenously is contra-indicated in patients with oedema who are thirsty. Those suffering from sulphonomide hæmaturia or anuria should receive intravenous water or glucose water without saline. It was a matter for speculation at first whether cases of pneumonia requiring intravenous fluids should not receive water rather than saline as only the provocation of diuresis was aimed at. However, the case histories reveal that $\frac{1}{2}$ N 5 per cent glucose saline was a most satisfactory intravenous solution for these cases.

In cholera it was noticed that patients treated with $\frac{1}{2}$ N glucose saline suffered recurrences of dehydration after improvement had taken place. In a severe case such episodes of severe dehydration recurred on 3 separate occasions within 2 days each time the rate of saline drip was slowed down because clinical signs of dehydration were overcome. On reviewing the cases it was suspected that N saline might have suited these patients better. On the other hand the

course of the illness with recurrent dehydration may have been merely associated with the gravity of the infection which was not overcome for the first few days. The point would be easily decided by estimation of the chloride content of rice water stools but unfortunately this was not done when cases were prevalent and the opportunity has not arisen again. However, of the 4 cases of cholera treated with this form of saline only one died and that not in the early dehydrated stage. It is not felt justifiable to recommend $\frac{1}{2}$ N 5 per cent glucose saline for use in cholera unreservedly until further cases have been studied. In all other conditions in which intravenous water and salt are required $\frac{1}{2}$ N 5 per cent glucose saline can be confidently used without fear of producing water or salt retention or deficiency.

Technique

Naturally the technique of preparation and administration affects results and therefore bare details are given below :

(a) The solution and all apparatus must be pyrogen-free and administration must be by a closed method, i.e. not by tube and funnel.

(b) The intravenous needle is inserted into a vein without incision.

(c) Veins in the forearm are used, not in the cubital fossa, and the forearm is supported in a vertical position against the stand by the bedside from which the saline flask hangs.

Summary

Physiological and clinical facts regarding water and salt metabolism are described. $\frac{1}{2}$ N 5 per cent glucose saline is considered to be a desirable solution for almost all kinds of cases requiring intravenous administration of these substances.

The details regarding fluid and salt balance in 36 cases on intravenous therapy with $\frac{1}{2}$ N 5 per cent glucose saline have been studied and illustrative cases are recorded. From a study of these records it is revealed that provided $\frac{1}{2}$ N 5 per cent glucose saline is used estimations of plasma or urine chloride are unnecessary. Only the urine volume, which depends on alimentary intake and output, intravenous intake and other subsidiary factors, need be recorded and studied with a view to estimation of intravenous requirements for the ensuing 24 hours.

A simple table for the estimation of the amount of $\frac{1}{2}$ N 5 per cent glucose saline required when the urinary volume is at various levels is appended.

Intravenous administration of salt is contra-indicated in oedematous, thirsty patients and is undesirable in cases of sulphonamide hæmaturia or anuria.

In cholera it is not certain whether $\frac{1}{2}$ N 5 per cent glucose saline is a satisfactory solution. In all other cases it is recommended that this solution should be administered as a routine.

I have pleasure in thanking Dr. W. B. Roantree, Chief Medical Officer, Kolar Gold Field, for his encouragement and advice, Dr. J. M. Daly for permission to include some of his cases, and Messrs. John Taylor and Sons (India), Ltd., the Managers, for permission for reporting.

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SQUAMOUS METAPLASIA AND KERATINIZATION IN CYSTIC HYPERPLASIA OF THE HUMAN BREAST

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THE histological appearances in cystic hyperplasia of the breast, the condition still commonly referred to as 'chronic mastitis', have been widely discussed. This case is reported to record a rather unusual degree of intraduct squamous metaplasia and keratinization.

Case history.—An unmarried woman of 40 years had noticed, ten months prior to admission into hospital, a small 'gathering' on the areola of the right breast discharging pus. After a course of diathermy, there was a blood-stained discharge. Clinical examination revealed bilateral 'chronic mastitis' with a small mobile sub-areolar swelling in the right breast. Small soft lymph nodes were palpable in both axillæ. A simple mastectomy was performed, and the patient made a good recovery.

The specimen received in the laboratory was a rather fat breast, showing slight retraction of the nipple and a sub-areolar, firm, yellowish, spherical nodule, an inch in diameter. Pieces taken for histology included the nipple, the nodule and the underlying breast tissue which looked normal.

Histology.—All the sections studied showed features of cystic hyperplasia (figures 1, 2 and 3, plate I). Some of the larger and many of the subsidiary ducts showed considerable dilatation, often frankly cystic, the desquamation, partial or complete, to hyperplasia. One of the most striking features was the complete replacement of the normal epithelium in some of the dilated ducts by stratified squamous epithelium, several cells in thickness, with keratinization at the surface. Laminated pink-staining material (H. & E.), the outer laminae consisting of keratin with some cellular debris, was seen in the cysts. Where the lining epithelium was desquamated, giant cells of foreign body type, with as many as 50 nuclei, were found along the inner surface of the cyst wall and in juxtaposition with the laminated material. The periductal connective tissue showed collections of lymphocytes and histiocytes with occasional polymorphs, though in some places plasma cells were prominent. In parts, the cells had infiltrated the entire thickness of the duct wall, reaching the epithelial lining. Similar cell collections were noticed in the interstitial tissue of the breast and in relation to normal ducts. The deeper parts of the sections presented features of intra-canalicular fibro-adenoma. Sections stained Gram, and treated with acid alcohol, showed varying amounts of keratin in the laminated material.

The condition was diagnosed as cystic hyperplasia with unusual features, and since an amputation had already been done, no further treatment was considered necessary.

Discussion

Epithelial metaplasia occurs in neoplastic as well as in non-neoplastic conditions. No specific causative factor is recognizable in the former, but in the latter, chronic inflammation, nutritional impairment and alteration in the function of the organ concerned are amongst the causes. It is also observed in conditions of disordered hormonal control. Squamous metaplasia in the glands is a frequent finding in endometrial cystic hyperplasia, the result of persistent oestrogenic over-stimulation, and in benign glandular hyperplasia of the prostate, particularly in stilboestrol-treated cases. Hyperplasia and metaplasia have been reproduced in experimental animals, in the latter organ, by oestrin and its synthetic substitutes (Burrows, 1935a).

In cystic hyperplasia of the breast, a condition generally accepted as resulting from disordered hormonal control, in particular an oestrogen excess, squamous metaplasia seems uncommon. Willis (1948) in his 'Pathology of Tumours' mentions that it is very rare in the breast, save in carcinomatous tumours, and observes that even here, it is rarer than might be expected, in view of the development of the organ from the ectoderm. Though changes in the human breast associated with cystic hyperplasia have been experimentally induced in animals by oestrogen, squamous metaplasia has not been observed frequently. Bonser (1945) saw it only on rare occasions in oestrogen-treated mice, but Kirschbaum *et al.* (1946) observed it constantly in mice of certain genetic types painted with methyl-cholanthrene.

The rarity of squamous metaplasia, in the relatively common cystic hyperplasia of the human breast, renders it necessary to seek an explanation, when it does occur, in factors other than hormonal. Retention of secretions with an alteration in their character would be a possible cause, but this would not be consistent with the rarity of metaplasia. Two factors, (a) infection and (b) deficiency of vitamin A, deserve consideration.

Squamous metaplasia of epithelial linings following suppuration is well known, the change in infected bronchiectatic cavities being a typical example. In the present case, the clinical history of a 'gathering' discharging pus would point to a suppurative process. Unfortunately, the discharge was not cultured for organisms. On microscopic examination, there was no active inflammation. The presence of lymphocytes and histiocytes, described in the histological report, is a common finding in cystic hyperplasia and does not necessarily denote inflammation at any stage, nor can the

cellular infiltration in the walls of the ducts, sometimes reaching the epithelial lining, be interpreted as due to pre-metaplastic inflammation. On the other hand, leucocytic infiltration seems to be an accompaniment of squamous metaplasia and keratinization (Burrows, 1935b).

Clinical and experimental evidence have made it clear that the fat-soluble vitamin A is necessary for the preservation of epithelial integrity. Widespread epithelial atrophy, followed by squamous metaplasia and keratinization, have been observed in animals maintained on vitamin A deficient diets (Wolbach and Howe, 1926), and in children suffering from similar deficiency (Blackfan and Wolbach, 1933). The findings in mice receiving oestrogen are even more significant. Removal of vitamin A from their diet hastened squamous metaplasia and keratinization in the coagulating gland and increased the degree of keratinization to a remarkable extent (Bonser, 1935). It would appear that the two factors act synergistically, and it is very likely that deficiency of vitamin A can induce squamous metaplasia in the human breast already under the influence of oestrogen excess.

Summary

A case of cystic hyperplasia with an unusual degree of intraduct squamous metaplasia is reported.

The known causes of squamous metaplasia are discussed.

It is suggested that deficiency of vitamin A can induce squamous metaplasia in the human breast already under the influence of oestrogen excess.

I am grateful to Dr. W. Goldie and Dr. G. M. Bonser for their advice. My thanks are due to Mr. J. Hainsworth for the photomicrographs.

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PULMONARY MONILIASIS

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For many years mycotic diseases of the lungs have been regarded as rare infections which were of interest to the specialists of high order

only, but the evidence that has accumulated during the past few years has changed this viewpoint. We now know that mycotic infections occur with sufficient frequency to justify their being considered in the differential diagnosis of every difficult and complicated pulmonary and systemic infection.

This is also important for the reason that of all the non-tuberculous infections the mycoses most closely resemble tuberculosis. Disease producing fungi grow slowly in the tissues, induce giant cell formation and frequently produce a state of tissue hypersensitiveness which is analogous to that occurring in tuberculosis.

Some of the mycoses such as moniliasis and aspergillosis are relatively mild diseases, while others like actinomycosis and blastomycosis have a mortality much higher than that of tuberculosis. As regards geographic distribution, some of these such as coccidiomycosis, histoplasmosis, etc., have a fairly fixed geographic distribution, while others like actinomycosis, moniliasis, etc., are endogenous infections and may occur at any time, in any climate and in any stratum of society.

Monilia fungus is found on fruits, dead leaves, old straw and wood. The infection follows the inhalation of contaminated particles, and is found especially among workers in dusty straw and in tea tasters in Ceylon. Infection in human beings is caused by *Candida albicans* which is a species of *monilia fungus*. It may produce lesions in the mouth, skin, bronchi or lungs, and may occasionally cause septicaemia, endocarditis, or meningitis.

Lung infection with this fungus may be extensive or may be localized, and it may take an acute form or mild form.

Its diagnosis must be made with considerable caution. The fungus causing pulmonary moniliasis can be isolated so frequently from the throats of apparently healthy individuals that the presence of the fungus in the sputum may be coincidental. The problem is further complicated by the fact that *Candida albicans* may be found in the sputum from patients with pulmonary tuberculosis, lung abscess, bronchiectasis, etc., as it is a frequent invader in bronchial and pulmonary diseases. The diagnosis of pulmonary moniliasis has therefore to be made with considerable caution, since the isolation of *Candida albicans* from the sputum does not justify in itself a diagnosis of moniliasis. It is warranted only if the fungi can be found constantly and in large numbers and on repeated examinations, in the sputum freshly coughed up from the lungs, and other aetiological agents are excluded.

The following three cases are reported because of the diagnostic problems and many unusual features presented by them :

Case 1

K. D., Hindu female, aged about thirty years, from Delhi, attended the out-patient department of this hospital on 25th May, 1949, for treatment. She had been diagnosed as a case of bilateral pulmonary tuberculosis at some other institution.

Family history.—No history of tuberculosis in the family either on the father or the father-in-law's side.

History of previous illness.—The patient gave history of typhoid fever when she was about ten years old, and of lobar pneumonia at the age of twelve or thirteen years. She also suffered from occasional attacks of nasal catarrh and tonsillitis during her childhood.

History of present illness.—In November 1947, the patient suffered from fever and cough which persisted for about three months and subsided under some homœopathic treatment. The patient became pregnant in the month of July 1948. She felt quite well during the first five months of her pregnancy. After that cough reappeared and persisted throughout the pregnancy in spite of all treatment.

The patient was delivered of a female child on 27th April, 1949. She developed high fever on 30th April and cough also got worse. She received some treatment at Delhi with which her fever came down but the cough persisted, and it gradually assumed the character of an asthmatic cough. It was productive but the sputum was sticky and came out with great difficulty. When the cough did not subside the patient was advised to go to hills for rest and proper treatment.

The patient went to Simla and was x-rayed on 20th May, 1949. On the basis of the findings of the skiagram she was labelled a case of bilateral pulmonary tuberculosis and was advised to join some tuberculosis sanatorium.

She came to Dharampore and was examined at the Hardinge Sanatorium on 25th May, 1949. At the time of examination her temperature was 102°F., pulse was 130 per minute, and the tongue was coated and moist. She had a slight vague pain in the chest and was dyspnoeic. She had cough which was harassing. There was no abdominal tenderness on palpation. Her weight was 98 pounds.

Physical examination of the chest did not show any dullness in any particular area, breathing was found to be broncho-vesicular in the mid-zones over both the lungs, and medium moist râles were heard over the areas of involvement.

Laboratory examinations.—Blood sedimentation rate was 7 mm. during the first hour. The white cell count was 7,500 per c.mm. Differential count showed polymorphs 62 per cent, lympho 24 per cent, large mono 4 per cent and eosinophils 10 per cent.

She had brought her skiagram taken on 20th May, 1949, at Simla, and the report accompanying it read as follows: Exudative form of pulmonary tuberculosis both lungs, all zones are involved. Trachea and heart are deviated to the right. Right costophrenic angle is blocked. Peaking of the diaphragm on the left side (figure 1, plate II).

The patient was given a bed in the waiting shed and was given a sterilized phial to collect her sputum, which was examined on 26th May, 1949, with the following findings: Quantity about one and a half ounce, whitish yellow with a purulent look, mucoid and gelatinous in consistence. Microscopical examination showed abundance of pus cells and secondary organisms. No tubercle bacilli were found even after a thorough search. A large number of small, oval, thin-walled cells was also present.

As no tubercle bacilli were found on the first examination, the sputum was examined daily for three days and the findings were the same, namely, that no tubercle bacilli were seen, while small, oval cellular organisms were seen in every slide (Gram's stain). Mantoux test was done on 31st May and was found to be negative.

On 31st May, a sample of sputum was sent to the Central Research Institute, Kasauli, for microscopical examination. The report was: 'The smears from the sputum show pus cells and epithelial cells. Streptococci, staphylococci, Gram-negative diplococci and organisms resembling morphologically *Monilia albicans* also present'.

As the patient had high fever and harassing cough, and as the sputum showed pus cells and a heavy secondary infection, she was put on a supporting, symptomatic treatment, and penicillin injections of 500,000 units daily in two morning and evening doses. This treatment was carried on for ten days. With this the fever came down to 100°F., the cough was slightly less and the colour of the sputum became less purulent. Weight was 99 pounds. There was a slight all-round improvement but it was not as dramatic as could be expected with this line of treatment. Her sputum was examined on 14th June, 1949, at Hardinge Sanatorium, and it again did not show any tubercle bacilli, but showed a large number of organisms resembling *Monilia albicans*.

A specimen of the sputum was again sent to the Central Research Institute, Kasauli, for thorough microscopical and cultural examination and the report received from there read as follows:—

Microscopic.—Epithelial cells and pus cells.

Gram-positive and Gram-negative cocci resembling streptococci, staphylococci, and *N. catarrhalis*.

Organisms resembling morphologically *Monilia albicans* present.

Cultural.—*Streptococci viridans*, staphylococci, *N. catarrhalis*, and Gram-negative slender bacilli (*H. influenza* ?) isolated.

Organisms resembling morphologically *Monilia albicans* isolated on Sabourraud's agar.

On 16th June, the organisms grown from the patient's sputum were tested against her blood serum. There was no agglutination in two hours and the reading next day was inconclusive, as the suspension had settled in all the tubes including control, so the agglutination test was found to be negative. A skiagram was taken on 16th June, 1949 (figure 2, plate II). This skiagram was compared with the one taken on 20th May, 1949, and it showed that the condition of the lungs was more or less the same with no appreciable difference.

These skiagrams were sent to Dr. George Politzer, M.D., M.M.R., for expert reading, and his report was as follows:—

'The case is roentgenologically not all too typical for tuberculosis. The strangeness in the picture is that the stripe and spot-shaped opacities are not connected with each other. Cases of this kind are sometimes found when primary fibrous changes as for instance in pneumoconiosis are getting, secondarily to some exudative, often non-tuberculous foci. But it is surely difficult to come to a clear diagnosis of such a case by x-ray only. If I would have seen the case, I would have surely drawn the attention to the strangeness of the picture and without excluding tuberculosis done all laboratory examinations to clarify the case'.

As no tubercle bacilli were ever seen in the sputum, and the Mantoux reaction was negative, and as *Monilia albicans* were found in abundance in the fresh sputum every time that it was examined, it was decided to diagnose the case as one of pulmonary moniliasis.

Before putting the patient on potassium iodide treatment, the organisms were cultured on Sabourraud's glucose agar media at this institution. The growth became evident in four days and showed medium-sized moist colonies, having a distinct yeasty odour. A few slides were prepared from this growth and the same were stained with Gram's stain. *Candida albicans* was found as small, oval, thin-walled cells, which showed budding. A few mycelial elements were found and the budding cells were seen attached to the hyphae at the point of constriction.

The patient was put on potassium iodide and gentian violet treatment. Five drops of saturated solution of potassium iodide (prepared by dissolving 480 grains of potassium iodide in one ounce of water) were given thrice daily in one ounce of water, the dose was increased by one drop daily till the patient was getting a dose of ten drops of potassium iodide solution thrice daily. She was also given 10 cc. of 0.25 per cent solution of gentian violet

solution (prepared at the Central Research Institute, Kasauli) by the intravenous route on alternate days. She was kept on sanatorium regime, and was also given multivitamin tablets twice daily.

The patient showed a marked improvement, the temperature came down to 99°F., cough was markedly decreased, and the expectoration came out easily. The pain in her chest disappeared and she felt a sense of well-being. Her weight showed an increase of three pounds in two weeks.

Her sputum examined on 30th June, 1949, showed that the 'secondary organisms and *Monilia albicans* were much less. Her blood sedimentation rate was now found to be 5 mm. during the first hour.

The skiagram of her chest taken on 30th June, 1949, showed a fairly marked improvement (figure 3, plate III) as compared with the skiagram taken on 16th June, 1949.

On getting some news from home she left suddenly for Pathankote. On 20th July, 1949, I got a letter from her doctor at Pathankote, in which he informed that her condition was better, and he asked for some more gentian violet ampoules for her. He also sent her latest skiagram but nothing of any importance could be made out.

Fifteen days later I got a letter that she was again getting fever, which was as high as 104°F., cough was severe and that she was seriously ill.

I again wrote a letter on 19th August, 1949, in which I requested the doctor to inform me about her condition and send me her new skiagram, to which I received a reply on 27th August, 1949, informing that the patient had died on 13th August, 1949.

Case 2

Mr. D. D., Hindu male, aged about twenty-two years.

Family history.—No history of tuberculosis in the family.

History of previous illness.—The patient suffered from dysentery at the age of twelve years which lasted for about two months, and even after that he felt some discomfort in the abdomen and loss of appetite for many months. He also suffered from occasional attacks of sore throat.

Five years back the patient suffered from severe itching all over his body and had urticaria, which did not yield to ordinary routine medication, and had to get ten injections of his own blood to get relief from the above trouble. The patient also suffers from frequent night discharges for the last seven years, which occur sometimes thrice a week.

History of present illness.—In the month of May 1949, the patient was at Banaras in railway

service, and he used to feel tired in the evening. A few days later he developed slight cough, and on 1st June he found that he had fever which at that time was 99.8°F. After that he always had fever in the evening and by 14th June the evening temperature was 101°F., and the cough also became more distressing. A skiagram of his chest was taken on 14th June at Banaras, and on the basis of the findings of that skiagram he was diagnosed to be suffering from bilateral pulmonary tuberculosis. I examined his skiagram and it read as follows: 'Medial halves of both the lung fields show increased pulmonary striations with marked bilateral hilar enlargement with coarse mottling and crowding of bronchi in both the cardiophrenic angles. There are two ill-defined ring-shaped shadows: one near the anterior end of the left third rib and the other near the anterior part of fourth right intercostal space'.

He came to Patiala and was put on streptomycin treatment on 17th June and was given a total of sixty grams of this drug in sixty days, in two morning and evening doses. A skiagram was taken on 17th August, 1949, at Patiala (figure 4, plate III) and it read as follows:—

'Fibrotic strands radiating from the hila towards the periphery of both the lung fields in their medial halves are well defined. Crowding of bronchi is seen in both the cardiophrenic angles. The coarse mottling at the bases and in the hilar and perihilar regions appear now as calcified spots looking like broncholiths'.

A specimen of his sputum was sent to the Central Research Institute, Kasauli, for examination (this being the first time that his sputum was examined) and the report received from that institution was as follows:—

'Sputum—negative to tubercle bacilli; *Candida albicans* plus plus'.

It was at this stage that the patient came under my observation through the courtesy of Dr. Gurmikpal Singh of the Central Research Institute, Kasauli.

His temperature in the evening did not rise higher than 99°F., cough was less, appetite had slightly improved, and there has been a steady gain in weight. The main trouble that he had now was slight dyspnoea on walking, general weakness, and irritation all over his body.

I examined his sputum and it showed *Candida albicans* in abundance, while it was negative to tubercle bacilli. On culture on Sabouraud's agar the growth was apparent on the fourth day, and slides prepared from this growth again showed the fungus.

I put the patient on potassium iodide and gentian violet treatment on 21st September, 1949. The patient showed marked improvement in his clinical symptoms. The fever came down to normal (occasionally 99°F.), cough was practically gone and so was the dyspnoea. There

was no breathlessness and the patient went for a walk daily.

His third x-ray picture was taken on 17th October, 1949, at Dharampore, and it showed more or less the same condition as was shown in the picture taken on 17th August (figure 5, plate IV).

His sputum was examined the same day and was found negative for tubercle bacilli (concentration method), but showed *Candida albicans* (Gram's stain). His blood sedimentation rate was taken and was found to be 5 mm. during the first hour.

Potassium iodide and gentian violet treatment has been stopped for the time being, and the patient is still under observation.

Case 3

Mr. Satya Paul, Hindu male, aged about twenty-five years.

Family history.—Father died of pulmonary tuberculosis when the patient was five years old.

History of previous illness.—The patient suffered from pleurisy at the age of ten years and from typhoid at the age of fourteen years.

History of present illness.—In February 1947 the patient had feeling of tiredness in the evening, a few weeks later cough appeared, and he also got fever in the evening.

A skiagram of his chest was taken on 12th March, 1949, which showed bilateral infra-clavicular lesions of exudative type with a cavity on the left side (figure 6, plate IV). Sputum was examined and showed the presence of tubercle bacilli.

The patient came under my treatment in April 1947. Artificial pneumothorax was tried on the left side but failed, so the patient was kept on general treatment and sanatorium regime. He made fairly good improvement clinically, and by the winter of 1948, the lesion in his right lung had cleared, and he was fit for thoracoplasty operation on his left side. Thoracoplasty was done at Lady Linlithgow Sanatorium, Kasauli, but he still remained a positive case.

He came back to me again in the summer of 1949. His sputum was examined and it showed tubercle bacilli. Except for the positive sputum the patient had neither fever, nor cough, nor any other clinical symptom. He was kept under observation on sanatorium regime.

One month later his sputum was examined and it showed tubercle bacilli as well as *Candida albicans* (Gram's stain). After that his sputum has always shown the presence of *Candida albicans* in large numbers, as well as tubercle bacilli. The patient has no clinical symptoms except slight hoarseness of his voice and slight inflammation of the vocal cords.

Summary

1. Three cases are reported in which *Candida albicans* were found in the freshly coughed sputum.

2. In the first two cases there has been great similarity in signs, symptoms and roentgen findings between pulmonary moniliasis and pulmonary tuberculosis which emphasizes the importance of care in making the correct diagnosis, which should never be based on roentgenological findings alone, but should be supported by laboratory procedures and other examinations.

3. *Candida albicans* can be found as a saprophyte or secondary invader in other broncho-pulmonary diseases like tuberculosis, abscess of the lung and bronchiectasis as seen in case 3.

My grateful thanks are due to Dr. Gurkirpal Singh of the Central Research Institute, Kasauli, for his help in doing some of the laboratory examination and supply of gentian violet ampoules and to Dr. Wazir Chand for referring the second case to me.

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CONTRA-LATERAL FRACTURE OF THE FIRST RIB FOLLOWING THORACOPLASTY

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IDIOPATHIC fracture of the first rib on the contra-lateral side has been mentioned as one of the rare complications of thoracoplasty operations.

Guggenheim and Bernard (1948) of the National Jewish Hospital at Denver reported that out of 208 cases who had thoracoplasty operations performed at the National Jewish Hospital at Denver, spontaneous fracture of the first rib was revealed in six cases and of first and second rib in two cases making an incidence of 3.8 per cent.

Of the 281 cases who had thoracoplasty operations in the Lady Linlithgow Sanatorium at Kasauli since 1941, idiopathic fracture of the first rib was noticed in two cases.

Case reports

Case 1.—R. C. P., female, aged 22 years, admitted on 29th January, 1949, with the complaint of repeated attacks of cold and cough with expectoration since July 1947. Two months later she started running pyrexia, temperature in the beginning was intermittent in character and later on remittent, varying between 100°F. and 102°F.

Skiagram of chest was taken in September 1948, which revealed a mixed type of pathology with a cavity in the upper and mid zone of left lung, right lung was clear, no abnormality of the first rib on either side (figure 1, plate V). Sputum was positive for tubercle bacilli, and she was diagnosed to be suffering from pulmonary tuberculosis.

She was admitted in the sanatorium on 29th January, 1949. A. P. was tried on the left side on 9th February, 1949, but was unsuccessful.

First stage thoracoplasty with apicectomy was done on 25th March. Post-operative course was uneventful except that she had pyrexia up to 102°F. Temperature started coming down from the 5th day of operation. Had some paradoxical movement of the chest wall with considerable difficulty in bringing out expectoration.

Skiagram done on 8th April, 1949, preceding the second stage of thoracoplasty revealed fracture of anterior third of the first rib on the contra-lateral side (figure 2, plate V). The patient had no symptoms and no treatment was given.

Case 2.—D. B., male, aged 26 years, admitted on 8th January, 1949, with history of cough with expectoration, duration 6 months and occasional blood-tinged sputum. After about one month started getting temperature with rigor in the evening. Skiagram of chest taken in November 1948 revealed predominantly exudative type of pathology with a big cavity in the upper and mid zone in the left lung, no abnormality of first rib on either side (figure 3, plate VI). Sputum examined and was positive for tubercle bacilli. Diagnosed to be suffering from pulmonary tuberculosis and admitted on 2nd December, 1948, in Military Hospital at Ranchi. He was on general treatment and subsequently transferred to Lady Linlithgow Sanatorium on 8th January, 1949.

A. P. started on 13th January, 1949, had six refills and it had to be abandoned on 29th January, because the collapse was contra-selective.

First stage thoracoplasty was done on 21st March. Post-operative course was usual but there was considerable difficulty in bringing out expectoration.

Skiagram done on 6th May, 1949 (figure 4, plate VI), preceding the second stage of thoracoplasty revealed fracture of the anterior third of the first rib on the contra-lateral side.

Patient had no symptoms, no treatment was given.

Discussion

Spontaneous fracture of ribs other than the first have been reported due to excessive cough in tuberculous patients (Stimson, 1883; Webb and Gilbert, 1923; Palfrey, 1924). These fractures are probably due to muscular stress and strain; but occurrence of fracture of the first rib is rather rare. This has been explained partly due to lack of interpretation of apical pathology, overlapping of shadows in that region and partly due to the condition being not borne in mind as it is never associated with any symptoms.

All the cases reported by Guggenheim and Bernard had fracture in the middle third of the rib except one who had fracture of the anterior third. In both of the writer's cases the fracture site was in the anterior third of the rib.

Out of the eight cases reported by the same authors, seven had complete fracture, one had incomplete, while both of the writer's cases had complete fracture.

In none of the writer's cases was there spontaneous fracture of the second rib.

Though great majority of fractures are due to accidental trauma, according to Lane (1887), isolated fracture of the first rib occurs due to one of the following reasons: (a) Indirect violence being transmitted through the clavicle, (b) directly by force applied from behind and (c) indirect violence being transmitted through the manubrium.

Spontaneous fracture of the first rib has also been reported (Oechsli, 1936). According to Bond (1945), decalcification of ribs and general debility may be one of the more important aetiological factors than muscular strain.

Position of patient during operation, tight bandage or application of sand bags have been considered as one of the predisposing causes but according to Guggenheim and Bernard removal of ribs during the first stage alters the normal mechanism of muscles attached to first and second rib on the contra-lateral side. The insertion of the scalenus anticus, medius and serratus anterior muscles is released when the first two ribs are cut, consequently pull of the corresponding muscles on the contra-lateral side is unopposed. This prolonged muscular tension may be responsible for the fracture. This view is further corroborated by the site of fracture which is close to the scalene tubercle where the bone is thin due to subclavian grooves.

Besides unopposed muscular action, difficulty in bringing out expectoration, paradoxical movement of chest wall and consequent dyspnoea may further aggravate this muscular traction on the non-operated side and thus causing fracture.

No complications such as pressure symptoms on nerves, or injury to blood vessels in the close

vicinity or tear of pleura were noticed in any of our cases.

Summary

1. Two cases of spontaneous fracture of the first rib have been reported on the contra-lateral side following thoracoplasty.
2. Fractures were symptomless and detected on routine x-ray examination preceding second stage.
3. No treatment was given.
4. Various ætiological factors have been discussed.

My thanks are due to Dr. H. N. Sahgal, M.B., B.S., T.D., officiating medical superintendent, for his kind permission for reporting these two cases.

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ORAL NOVOCAINE THERAPY IN PEPTIC ULCER

A STUDY OF 20 CASES

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Introduction

A BRIEF extract in a British medical periodical from Rougues's original article in *Presse Medicale* of Paris forms the basis of the following study. Recently Jocolli and Zambbelli in *Minerve Medica* of Torino and Filippi in *Presse Medicale* have published the results of their observation on a similar study but we have not yet come across either the original or any extract of their reports. Thus we would venture to suggest that except in its basic fundamentals the work is entirely our own, the details of investigations, therapy and regime

having been worked out independently under the guidance of our chief.

Rougues's method and observations.—Rougues records his study of 40 cases of peptic ulcer in which he tried this new method of treatment which consisted of the daily administration by mouth of 100 cc. of a fresh solution of 1 per cent novocaine taken in sips on waking up in the morning. The patient lay in the moderate Trendelenburg position, then right lateral for gastric ulcers, and frankly lateral for duodenal. The decubitus was maintained for one hour after completing the imbibition of the solution which occupied about 20 minutes. In some cases he gave divided doses, in equal parts, one in the morning and one in the evening. Pain was relieved in all but one case, and marked amelioration of symptoms was noticed for the first two days after which the condition yielded rapidly to treatment. Except in one case he got radiological evidence of reversion of ulcer and in one he noticed complete disappearance of the ulcer crater after 1½ months' treatment. The full duration of treatment was not mentioned.

Our interest.—We were impressed by Rougues's study, the simplicity of the therapy and the dramatic results he claimed in a disease which is so widely common in our part of the country. One meets in the out-patient departments and in the wards quite a large number of cases of peptic ulcer, duodenal and gastric, with and without pyloric stenosis, recent and old standing, and with evidence of malignant transformation. The relief given by the alkalis is not always encouraging and the results of the various surgical procedures leave still much to be desired. The morbidity and the economic handicap associated with the disease, the lethal complications during its course and the incidence of recurrence after medical or surgical treatment remind us that the cure for the disease is still to be sought elsewhere, that the medical profession has still to work for it in the wards, in the operation theatres and in the research laboratories all over the world. This study is probably one such attempt, a humble effort to solve the great problem. It needed no elaborate procedures or intricate apparatus, the economic factor was almost negligible and the relief in most cases was dramatic and sure. The patients when they left the wards, or when they subsequently reported at the end of the course, were grateful for the relief they got of the pain which in some cases had defied the physician's drugs and surgeon's knife.

Method: 1. *Selection.*—We made a definite selection of cases for the therapy. Obliteration of the pain in an ulcer with malignant tendencies would lead to disastrous results so that our cases were selected from the pre-cancerous age. Arbitrarily we fixed it at forty, so that all our cases were below this age. Again, cases with pyloric stenosis as evidenced by the visible peristalsis were reserved for surgery.

2. *Investigations.*—The following investigations were carried out before the patient was admitted for treatment:

- (i) complete hæmatological analysis;
- (ii) examination of motion for cysts, ova, and occult blood;
- (iii) fractional test meal; and
- (iv) barium meal series.

Type	Number
Duodenal	17
Anastomotic	3
Gastric	—
Total ..	20

Investigations	Number of cases
Anæmia ..	nil
Ova, cysts in motion	nil
Occult blood ..	3
F.T.M.—Normal ..	5
Hyper ..	15
Hypo ..	nil

If the motion showed cysts or ova, the treatment was to be given to rule out these as the cause of the symptoms and as the cause of occult blood. In the series of cases studied no case showed cyst or ova on repeated examination of the motions.

Admission and observation.—When the diagnosis had been definitely established the patient was admitted to the ward and observed for three days. A special chart was put up in which daily entries were made of the time of food, the time of onset of pain and the time it disappeared, for all the hours when the patient was awake.

Treatment.—The treatment began on the 4th day of admission. One gm. of novocaine powder was dissolved in 100 cc. of water and the patient sipped it slowly. After the first one or two sips the patient was observed for five minutes for evidence of any novocaine sensitivity after which the rest of the fluid was allowed to be sipped, the whole procedure taking nearly 15 minutes. This solution was taken as the first thing in the morning. He was then asked to lie down on his right side for one full hour. We have not insisted on the Trendelenburg position as in Rougues's cases. Entries were made in the chart regarding the time of onset of the pain and its relief as before.

Duration of treatment.—In every case whether the relief of pain was earlier or not the treatment was continued for 15 days at the end of which assessment of the results was made. If the pain had completely disappeared and there were

no other symptoms, no further novocaine was administered. If there was still occasional pain or heartburn, the treatment was continued for another week at the end of which a re-assessment was done and treatment stopped or extended for another week, as was found necessary.

Check up after treatment.—After the end of the therapy F.T.M. and barium meal series were again done and also the hæmatological analysis and examination of the motion in cases which had showed occult blood before, not due to parasites or diet.

Diet.—From the time of admission till the end of the first stage of treatment the patient was put on a bland hospital diet of bread and milk. Later he was allowed to take rice and curds with moderate quantities of condiments.

Ambulant patients.—Some of the patients of the educated and cultured type were allowed to go home after the first one or two days of commencement of treatment and advised to carry on with the treatment at home. One gm. packets of novocaine powder were given to them with instructions to dissolve one in 3½ oz. of water and sip in the morning as they did in the hospital. They were asked to make the subsequent entries in the chart where the earlier entries were already made during their stay in the hospital.

The cases.—This report is based on the first 20 cases although subsequently nearly an equal number had the same treatment in our unit.

Age.—The youngest in our series was 17 years old and the oldest 35 years.

Sex.—All the twenty were males.

Social type.—All were of the working class type except three who belonged to the lower middle class. Every one of them had his own anxieties and worries, domestic, financial, etc.

Family history.—Two gave peptic ulcer history in the family.

Complaint.—All of them came for pain in the abdomen with definite relation to food. Five had vomiting, none had hæmatemesis, 5 had medical treatment in other hospitals, 8 had indigenous methods of treatment, 3 had operations (gastro-jejunostomy) done on them formerly, 4 complained of acid eructations and 18 of loss of weight.

Duration.—The minimum was three months and the maximum 11 years.

Investigations.—(1) Blood investigations revealed no anæmia in any of the cases or any eosinophilia to suggest parasitic infection. (2) Motion examination showed no ova or cysts in any of the cases. Three cases were positive for occult blood. (3) F.T.M. showed increased acidity in 15, in 5 normal, low in none, 12 showed mucus in specimens suggesting gastritis. No blood was seen in any specimen. (4) Barium meal showed irregularities of duodenal cap in all, 3 showed gastro-jejunostomies, being

cases of anastomotic ulcer. None in the series was a gastric ulcer case.

Treatment.—In 4 cases the treatment had to be extended beyond the first stage of two weeks. The maximum period was one month. Two cases were treated by the ambulant method, the rest of the patients being in-patients.

Results.—Seventeen cases got complete relief, 2 had recurrences, 1 had no relief at all. Those who had recurrences were readmitted and given another course of novocaine treatment and got complete relief. The one who had no relief begged for operation. No ulcer was found on laparotomy, but the appendix was found to be suggestive of chronic inflammation. Its removal gave him complete relief from symptoms. In the series only two had slight exacerbation of symptoms during the first one or two days of treatment and none showed any sensitivity to novocaine. The amelioration of the symptoms was noticed from the third day.

F.T.M. showed a definite lowering of acidity in every case. Barium meal pictures were not so conclusive. The irregularities were still there. In one, however, the radiologist reported after spot radiography that the stomach showed evidence of hypotonicity.

We could divide the cases into two classes, those who got dramatic relief from pain within a few days and those who got gradual relief from the symptoms. Cases with family diathesis of peptic ulcer and those who used to get very frequent and severe pain were those who got the dramatic relief. It had no relation to the duration of the complaint. In those who got gradual relief the first symptom to disappear was pain and the last to disappear was the heart burn.

Our two earliest cases who were treated in May 1947 are still free from complaints. One wrote and reported of recurrence and we advised him to undergo another course of novocaine therapy. Of the others we could follow up only ten cases.

Control.—Two cases were kept as control and were given identical conditions of diet and rest but no novocaine. At the end of 15 days they had no amelioration of the symptoms.

Discussion: (1) *How the novocaine acts.*—Rougues could not explain how exactly the novocaine brings about the relief or cure of the peptic ulcer. We too have made no definite progress in this direction so that the following explanations would remain hypothetical conjectures: (a) By its direct action on the exposed ulcer surface producing an analgesic effect. Pharmacology is against this, since to get such an effect a 10 to 20 per cent solution would be necessary. (b) By reducing the acidity. This could be done in two ways: by being an antacid which it is not, or by its inhibitory action on the oxyntic cells, this latter remains to be proved. (c) By reducing the tone of the stomach wall. A hyper-

motile stomach is more prone to ulceration. The atonia of the stomach produced by vagotomy and subsequent healing of the peptic ulcer may be considered as a similar process although the main effect of vagotomy is to cut off the psychic stimuli to the acid-secreting mechanism. (d) By its absorption by the blood stream and later action on the acid secretion. (e) By its action on the central nervous system and intercepting the acid-secreting stimuli. Comparison with vagotomy is suggested again.

(2) *Comparison with other methods of treatment.*—Novocaine therapy is not advocated as one to replace the well-established methods of surgery. However, it may be considered in those cases where the patient may not have the facilities to undergo the usual prolonged medical treatment, because of his work or temperament or economic position and for those who are unwilling to undergo any kind of operation. It could also be used as an adjunct to surgery. The patient would get considerable relief from his agonizing pain if during the rather prolonged waiting for the routine investigations he is given a course of novocaine. Professor R. Mahadevan recently mentioned this in a case of gastric ulcer where the patient's condition was too poor to risk a partial gastrectomy and a gastrostomy was done and 0.5 per cent novocaine introduced into the stomach daily. This gave the patient freedom from his excruciating ulcer pain and subsequently after the general condition improved the patient was subjected to a partial gastrectomy.

(3) *Defects.*—There are obvious defects in this work: the gaps in the investigation, which should include gastroscopy in every case and the difficulty of getting patients who would wholeheartedly co-operate both during treatment and subsequently in the follow-up studies. Visualization of the ulcer in every case by gastroscopy is an ideal aimed at but not yet achieved. Many patients while undergoing the treatment do things which would vitiate the results. Smoking cigars on the sly and taking forbidden food are not things the medical man or the nurse can always prevent. It is rarely that people report when they have got cured of their ailments. If they have not they reject the doctor and seek relief elsewhere.

Conclusions

This may be considered a preliminary report on a simple, easily available and easily administrable therapy in a disease that is incapacitating and sometimes death-dealing by its complications. The method has given cure or relief in most of the cases when properly selected.

We are greatly indebted to Prof. Raghavachary under whose guidance this work was done. Our thanks are also due to Dr. P. Arunachalam, Superintendent, Stanley Hospital, for the many facilities he made available for this study.

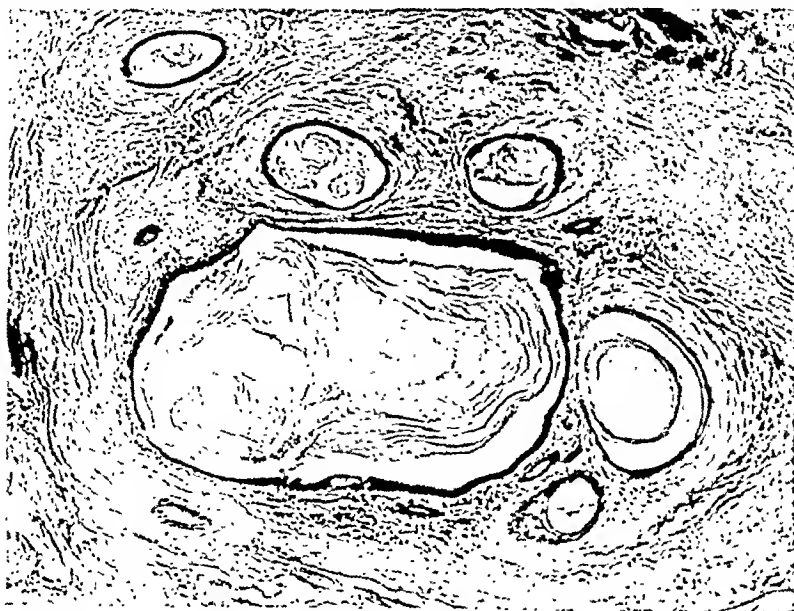


Fig. 1 ($\times 60$).



Fig. 2 ($\times 320$).



Fig. 3 ($\times 320$).



Fig. 1.

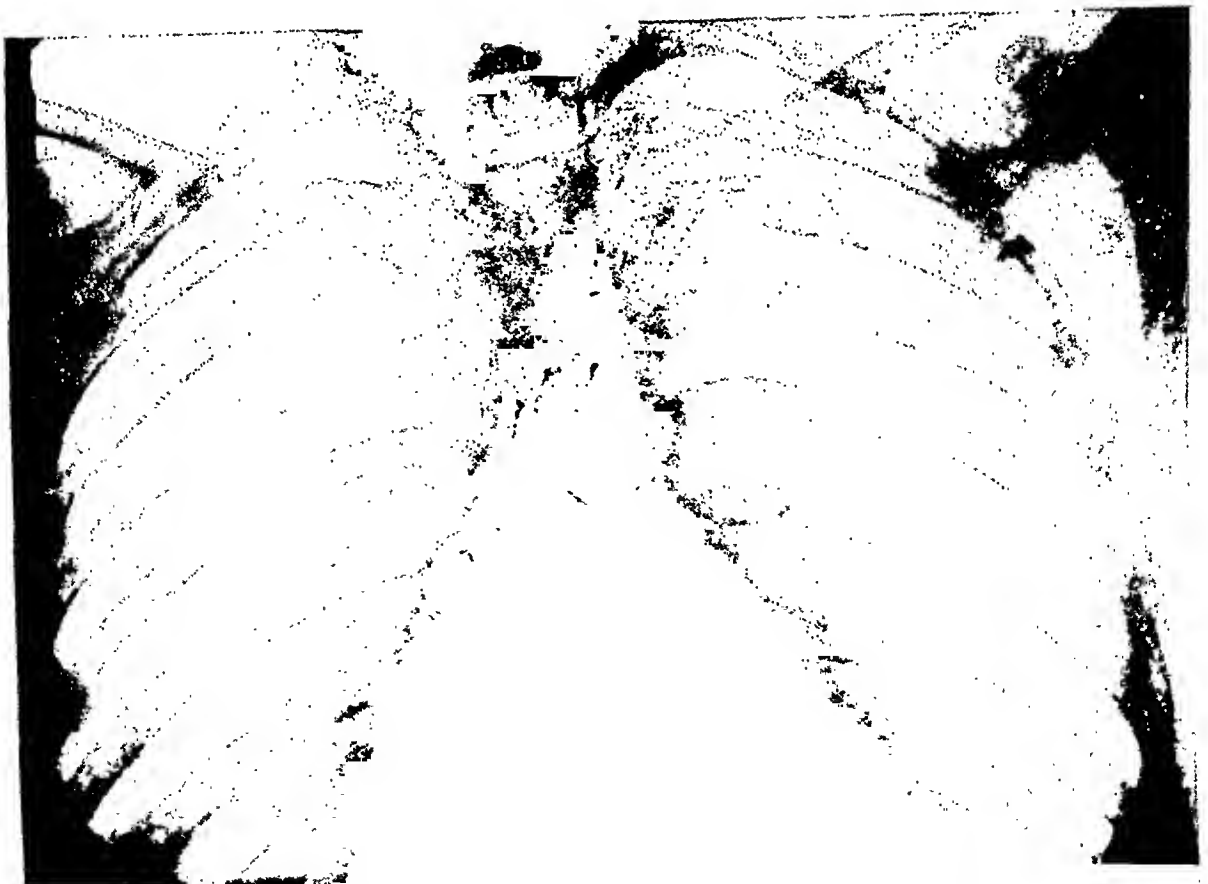


Fig. 2.

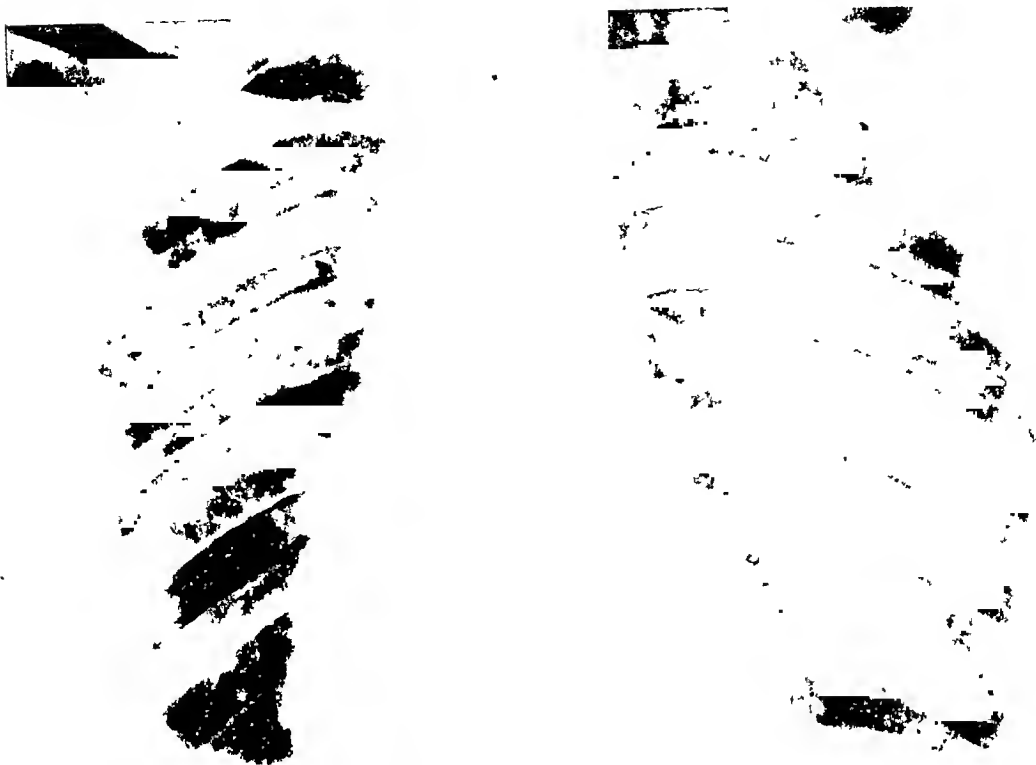


Fig. 3.

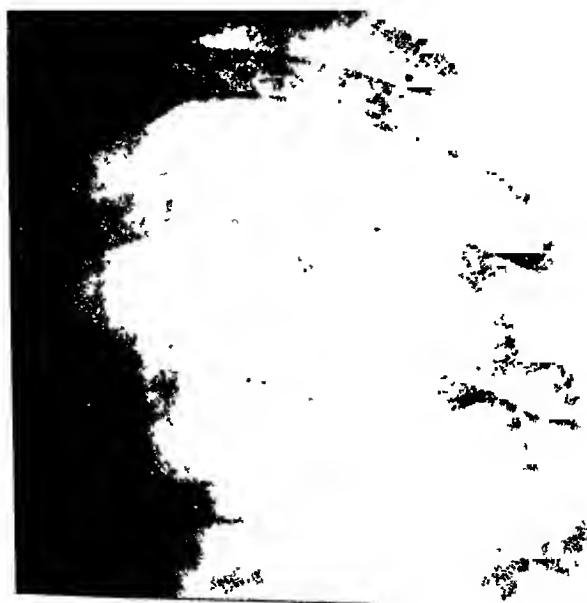


Fig. 4.

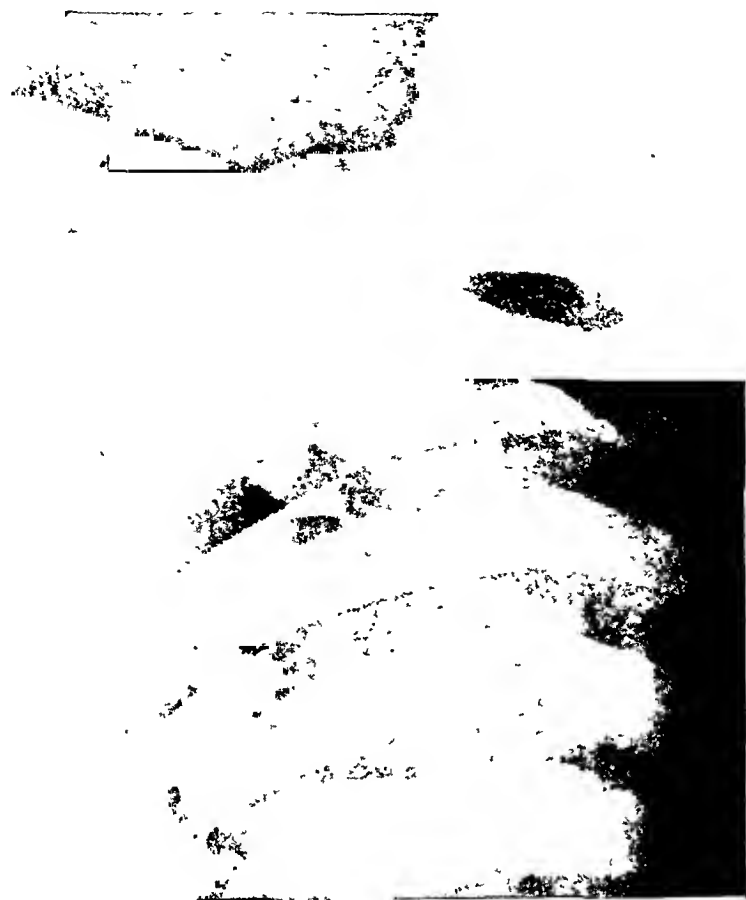


Fig. 5.

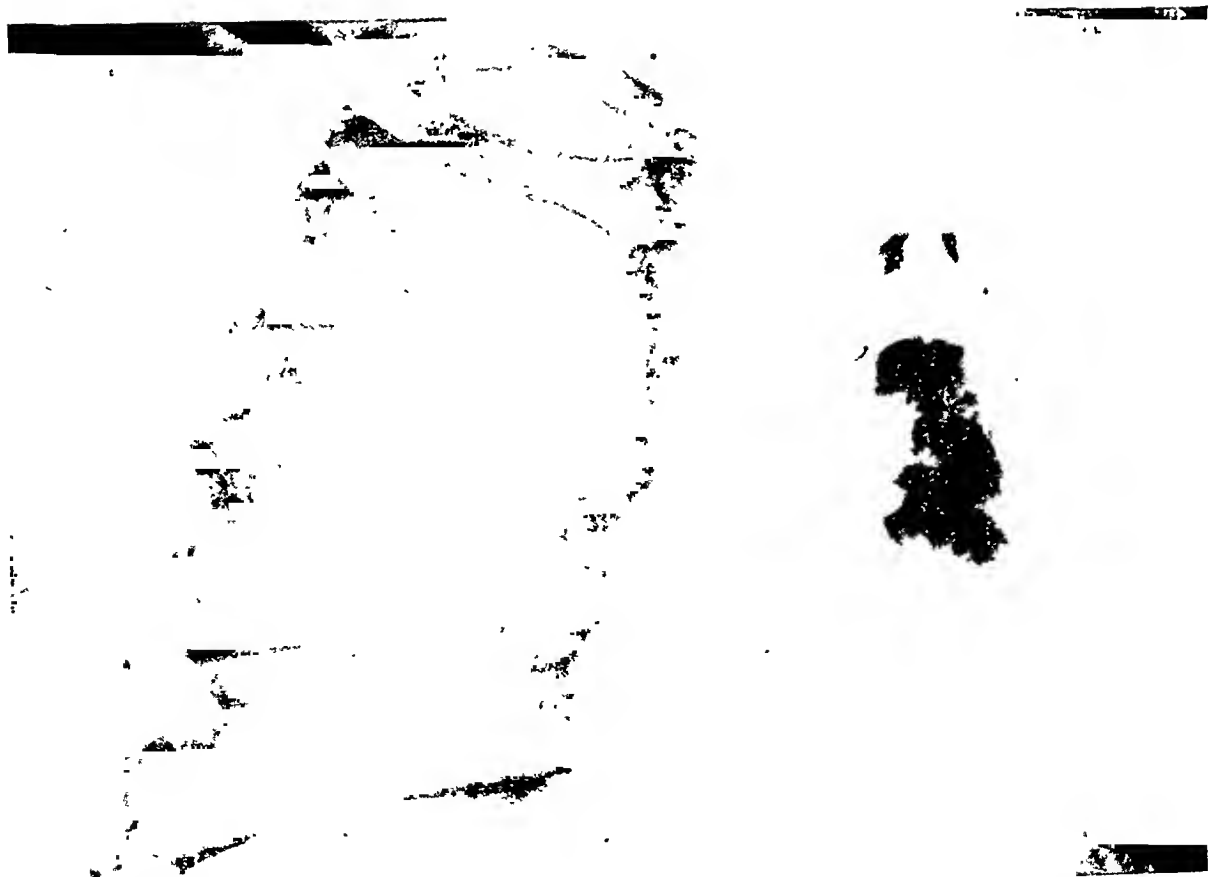


Fig. 6.



Fig. 1.



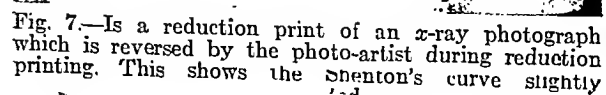
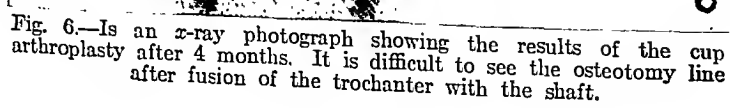
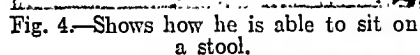
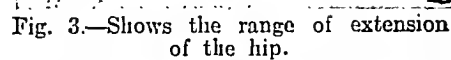
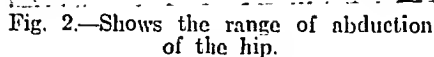
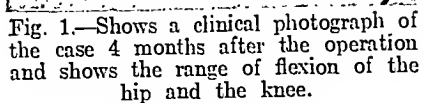
Fig. 2.

PLATE VI
CONTRA-LATERAL FRACTURE OF THE FIRST RIB FOLLOWING THORACOPLASTY : H. B. DINGLEY.
(O. A.) PAGE 14



Fig. 3.





CUP ARTHROPLASTY IN HIP JOINT SURGERY

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INFLAMMATIONS of various sorts occur in the hip joint. Traumatic conditions damaging the head, neck of the femur and the acetabulum are also commonly found. These lead to limitations of movement initially and later to fixity of the joint, ultimately ending in bad deformity. The resulting deformities due to neglect and ignorance afford opportunities for advanced surgery on the hip joint. Fixity and bad deformity cause great inconvenience especially among Indians who are accustomed to squat on the floor.

Infective arthritis of the hip resulting in ultimate fixation of the hip, arthritis of infants causing absorption of the head and neck resulting in shortening of the limb with a pathological dislocation, Perthes' disease which causes changes in the head and neck, various types of traumatic dislocations of the hip which after reduction lead to osteo-arthritis, central dislocation of the hip causing osteo-arthritis in most cases, unreduced dislocations of the hip and ununited fractures of the neck of femur—all these afford serious problems. Tubercular disease of hip is not included in this paper as it is a problem by itself. The following disabilities may occur:—

From very slight diminution of movement to complete fixation with a deformity varying in type and associated with pain is a constant feature. Of these sequelæ Perthes' disease and osteo-arthritis afford special problems which under modern conditions are amenable to treatment to improve the range of movement and get rid of pain.

Many operations have been designed, of which oblique osteotomy of McMurray, arthrodesis, arthroplasty and reconstruction of the hip are the methods employed with the object of—

- (a) abolishing the pain,
- (b) increasing the mobility of the hip in some cases, and
- (c) improving the functional value with stability by altering the axis for weight bearing.

In McMurray's osteotomy, in addition to correction of deformity, absorption of osteophytes occurs in cases of osteo-arthritis perhaps due to mobilization of calcium from these osteophytes during the healing of the fracture in this type of osteotomy.

All these operations have abolished pain and in some cases increased mobility and in most cases stabilized the hip after correcting the deformity. In recent times, Smith-Petersen

(1948), a pioneer worker in advanced hip joint surgery, has introduced a new operation of cup arthroplasty. His technique of exposure of the hip joint is too well known and requires no repetition. However, a few personal observations in technique deserve special mention. A large number of cases deserving this type of operation was seen in Madras but it was difficult then to get the necessary vitallium cups. However, early in January 1948, vitallium cups of various sizes were imported from America and opportunities occurred to try cup arthroplasty.

The first case tried was in a young man aged 25 years who had suffered from Perthes' disease early in life causing changes in the head and neck of the hip. He sought advice for

- (a) pain in the hip,
- (b) limitation of movement markedly in internal and external rotation and also in flexion and abduction, and
- (c) fatigue after walking which interfered with his occupation as a canvassing agent.

X-ray showed a flattened mushroom-shaped head (figure 5, plate VII). He was advised cup arthroplasty to which he consented and the operation was performed with the technique given below:

Lateral incision of Jones' type was used and the gluteus maximus was split in the direction of its fibres exposing the great trochanter with the attached muscles and the upper part of the origin of the vastus lateralis. The latter muscle was detached and the upper aspect of the femur 2 inches below the lower margin of the great trochanter was defined. The trochanter was sliced taking a big chunk of bone with the attached muscles displaced upwards. The front and posterior aspect of the neck was carefully defined and the capsule was cut on the antero-superior surface in the axis of the neck and the hip dislocated. The head was trimmed and cartilage removed with a Jones' broad gouge and the end smoothed with a file having no special reamers for this purpose. A vitallium cup fitting snugly on to the head and neck without constriction and pressure was selected and used. The great trochanter was wedged into a chink prepared by raising a thin ledge of bone on the lateral aspect of upper end of shaft of femur at a lower level and fixed by thick linen thread sutures through drill holes to the shaft of the femur. The capsule and the muscles were carefully sutured with linen thread. The wound was sutured in layers and the limb was put in plaster of paris in slight abduction. The patient made an uneventful recovery. The sutures were removed at the end of a fortnight and the plaster at the end of six weeks.

Discussion

Smith-Petersen's (1948) cup arthroplasty is a distinct advance and is definitely useful in

restoring movement in hip joint surgery. According to his technique and approach the trochanter is untouched. It is pointed out that after trimming the head to the required extent there is shortening of the neck thus altering the mechanics of the hip joint. This becomes evident by a study of the Shenton's line in radiograms seen in the pictures. Such being the case it is surmised that prolonged weight bearing will cause a certain amount of disability due to strain on the glutei. Therefore it was thought advisable to modify this operation by using Jones' technique of approaching the joint as in the case of pseudo-arthritis and giving a lower insertion to the glutei to restore the Shenton's line to as far as possible to normal, to give a better 'point de appui' and thus improve

the mechanics of the joint. In the case under report there is a slight exaggeration of the curve of Shenton's line (figure 7, plate VII).

This case is reported to show the results of such an attempt 4 months after operation (figures 1, 2, 3, 4 and 6, plate VII). This range will improve with function.

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A Mirror of Hospital Practice

SEXUAL DISORDER IN 'MEPACRINE PSYCHOSES'

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and

P. R. DAS GUPTA, D.T.M.

Simla

THE development of violent mental psychoses following administration of mepacrine in a small percentage of patients suffering from malaria is now an established fact. Quite a large number of such cases have been reported in the medical press.

So far as our information goes, no case has been reported where such mental symptoms developed following administration of mepacrine for the treatment of intestinal infestation by giardia. We have had the opportunity of dealing with two such cases. One case (case 'A') was seen and treated by one of us (K. B. K.) at Lahore in 1946 and the other case (case 'B') was seen and treated by both of us recently (September 1949) in Simla. A summary of the main symptoms, laboratory findings, other investigations, treatment and ultimate outcome is detailed below:—

Case 'A'

Hindu male, 36 years, married, thin built, insurance agent by profession, temperamentally of a highly strung and nervous nature, leading a very unhappy domestic life. He had attempted suicide three times.

The patient suffered from frequent attacks of diarrhoea for two years. Repeated stool examination showed giardia infestation. He was treated by a colleague with mepacrine one tablet t.i.d. On the 4th day (after having

taken 11 tablets of mepacrine) the patient was observed to be more talkative and a little outspoken by his wife. He passed rather restless night and was mostly awake. The mepacrine treatment was continued. The symptoms were aggravated by the afternoon of the following day (after 14 tablets had been taken). The patient was extremely talkative discussing every conceivable topic. He was however neither aggressive nor abusive. The patient was examined by one of us (K. B. K.). After greeting the doctor with unusual eloquence and formality he suddenly slipped into a discussion regarding widely different subjects and at times became incoherent. He talked very highly about himself and specially about his sexual powers and capacities. He appeared excited, his conjunctivæ were injected and face somewhat flushed. There was no yellow tinging of skin or conjunctivæ. Tongue appeared moderately coated and moist. Temperature, pulse, respiration, etc., were all within normal limits. Blood pressure was somewhat raised. Blood examination showed total and differential white cell count as well as total R.B.C. and hæmoglobin to be within normal limits. Urine showed presence of traces of mepacrine. (Exact figures are not given on account of the loss of records in Lahore.) No other abnormality was observed.

Treatment given.—Mepacrine was stopped. The patient was given one ampoule of Dial (Ciba) intravenously (0.2 gm. in 2.3 cc.). The patient remained as boisterous and talkative. He showed signs of extreme sexual excitement as indicated by the fact that he tied down his wife to a bed and repeatedly forced himself on her till she swooned. He had to be removed forcibly. Dial, one ampoule (0.2 gm.), was

repeated intravenously after six hours and the patient fell off to sleep half an hour afterwards. He woke up after about two hours and was as boisterous as before. Two tablets of Dial suspended in milk were administered and repeated after six hours. Patient then slept for short intervals off and on during the day and by night he was much less talkative, but was still incoherent in his speech. He was given another intravenous Dial (0.2 gm.) and he slept for about 4 hours. The patient was then kept on Dial tablets in gradually decreasing doses for about 15 days, after which period the patient appeared fairly normal in his speech, behaviour, etc. He however felt extremely weak and remained in bed for about seven days afterwards.

In another week's time he was up and about pursuing his normal avocations. He could recollect most of his doings during his illness and felt ashamed about them.

He however committed suicide by taking opium following domestic unpleasantness four months afterwards.

Case 'B'

Bengali Brahmin, male, aged 52 years, weight 136 lb., height 5 feet 6½ inches, widower, accountant by profession and 'of a highly strung and nervous nature'.

The patient suffered from attacks of diarrhoea off and on for the last 20 years, was at one time diagnosed to be suffering from chronic colitis of unknown origin. Residence in Bengal, his home province, aggravated this condition, but stay in the Punjab improved his intestinal condition and general health.

An attack of violent diarrhoea (15 to 20 watery stools in 24 hours) occurred every year during the rainy season necessitating his absence from duty for a period of a week or so every time. The use of Kapectate (Upjohns) and other anti-diarrhoeic medicines usually relieved this condition in about a week's time.

Laboratory findings: (1) *Stools*.—Stools were examined frequently during the quiescent period but no ova, amœba, cysts or pus cells were ever found. During the last attack of diarrhoea stools were examined and numerous cysts of *Giardia intestinalis* and *Trichomonas hominis* and a few pus cells were found.

(2) *Urine*.—It showed presence in traces of mepacrine and a faint trace of albumin.

(3) *Blood*.—Total R.B.C. 4,850,000 per c.mm. Hb. 96 per cent (100 per cent = 14.5 gm.). Total W.B.C. 6,800 per c.mm. Differential leucocyte counts—neutrophils 62 per cent, lymphocytes 28 per cent, monocytes 6 per cent and eosinophils 4 per cent.

The patient was advised to take mepacrine one tablet three times a day for five days and bismuth-kaolin mixture was prescribed in

addition. The intestinal condition improved rapidly. On the 3rd day the patient complained of hyperæsthesia of the skin all over his body, most marked however over the extremities. This condition worsened on the 4th and 5th day. On the fifth day of treatment (by which time he had taken 13 tablets of mepacrine) the patient showed signs of moderate restlessness. Later in the evening he looked excited and was rather talkative. He indulged in hurling vituperations at his children and on occasions burst into bouts of laughter without any rhyme or reason. He did not sleep during the night and his condition deteriorated by the following morning. He talked incessantly on various subjects and was very incoherent. He showed signs of sexual excitement and was found to take delight in discussing sex matters specially with the female members of his household. His penis was observed to be erect all the time and on one occasion he showed definitely erotic behaviour towards his own daughter-in-law. He was examined by us on the 6th day. Mepacrine treatment had already been discontinued as the prescribed course had been completed. The patient's general condition and behaviour were as described above: very talkative, incoherent, excited and abusive. There was no yellow tinging of skin or conjunctiva.

Temperature 98.2°F., pulse 78 per minute, respiration 19 per minute, blood pressure—systolic 152 and diastolic 80.

Treatment.—He was given one ampoule of Dial (Ciba) intravenously straightway. After half an hour of administration of Dial the patient became somewhat quieter. One ampoule of Dial was repeated after six hours intravenously. After an hour of the second dose the patient slept for two hours and on waking up he appeared less excited but still incoherent. He was given Theogardenal gr. 1 h.d. and a sleeping draught containing 30 gr. of sodium bromide and 15 gr. of chloral hydrate at 9 p.m. every night. In addition he received 2 cc. each of Crude Liver Extract and Vitamin B Complex (T.C.F.) daily by the intramuscular route for ten days. During this period the doses of Theogardenal as well as the bromide and chloral hydrate were gradually reduced and eventually given up after 15 days. He made an uneventful recovery. His memory after the period of mental disorder was intact and he could recollect to a great extent his actions and felt ashamed of himself.

Summary

1. Two cases of temporary mental disorder following mepacrine administration in patients suffering from giardia infestation are described.
2. There seem to be no premonitory symptoms or indications which would enable the physician to anticipate the advent of mental

symptoms in any particular patient under treatment with mepacrine. It is significant, however, that both of the cases were of 'highly strung and nervous nature'.

3. Intense sexual excitement was a marked feature in both the cases, cause of which needs further investigation.

4. The part played by Crude Liver Extract or Vitamin B Complex or both is difficult to assess. A bigger series of such patients must be investigated before a definite opinion can be

given. (Case 'A' was treated without and case 'B' treated with Liver Extract and Vitamin B Complex, but the rate of recovery was practically the same and the ultimate outcome was also similar.)

5. Both the patients recollected to a fair extent their unusual behaviours during their illness. This is in contrast to what some other workers have reported with regard to mental psychoses following mepacrine administration for the treatment of malaria.

Occasional Notes

THE VENEREAL DISEASE PROGRAMME OF THE WORLD HEALTH ORGANIZATION

THE SIMLA TRAINING CENTRE AND DEMONSTRATION AREA

PRESENTATION by JOHN C. CUTLER, M.D.

Venereal Disease Demonstration Team of the World Health Organization; Simla Branch of the Indian Medical Association, Simla, India, 29th June, 1949

As an introduction to the discussion of the venereal disease activities of WHO, it may be relevant to review briefly the aims, activities and accomplishments of the organization. The aims of the organization may be best summarized by a quotation from the constitution as 'the attainment by all peoples of the highest possible level of health'. The WHO was set up as one of the specialized agencies of the United Nations a little more than two years ago. From the beginning it was apparent that the health problems of the world, particularly in the under privileged and war devastated areas where funds, equipment and personnel are limited, are myriad.

The organization set out to carry out a programme in several fields. The demonstration and consultation services to governments provide for medical assistance in four major fields: Venereal Disease, Malaria, Tuberculosis, and Maternal and Child Health. The first three were chosen as being among the more widespread and serious of diseases which extract a fearful toll of life in addition to disabling men and removing them from productive work over long periods of time. Yet advances during the recent years have provided the medical profession for the first time in history with methods which make it possible to think in terms of control of these diseases on a large scale at a relatively small per capita cost. It was felt that aiding governments in their work in the

four fields mentioned, by means of demonstration teams, would be a most effective way to take advantage of existing knowledge.

Besides the actual medical assistance, the organization undertook to carry on some of the programmes of the League of Nations in epidemiologic reporting, standardization of medicinal products, etc., and to inaugurate a programme of collection of vital statistics.

As an adjunct to the activities already discussed, an intensive programme of educational activity was begun which comprised both granting of fellowships and publication of material of both general and specific public health importance. There have already been very concrete demonstrations of the value of international co-operation in health work. 'In the cholera epidemic in Egypt WHO's assistance to the Egyptian public health authorities . . . perhaps demonstrated most graphically how nations can co-operate against a common disease danger' (Calderone, 1948). Malaria control work has already shown results in Greece, the WHO Field Service through its activities has reduced the malaria incidence from 85 per cent to 5 per cent in the area where it operated. In many countries, including India, teams furnished by the Scandinavian Red Cross Societies under the ægis of UNICEF and WHO have been carrying out an extensive programme of B.C.G. vaccination for the control of tuberculosis. This simple measure had been proven to reduce the incidence of new cases of tuberculosis by about 80 per cent. The governments of Poland, UNICEF, and WHO carried out with penicillin the first nation-wide mass attack on syphilis in history with striking results. The experience has provided information as to effective means of combating similar situations in other countries. In about 10 months, 43,000 cases of syphilis and 27,000 of gonorrhœa were found and treated with penicillin as a result of mass testing.

The experience with penicillin therapy, in more than 500,000 patients treated for syphilis in U.S.A. alone, has shown that penicillin therapy is an effective tool for the public health control of syphilis. The patient is rapidly rendered non-infectious, and the short time required for treatment, coupled with an almost complete lack of serious toxicity, makes possible within a short time the completion of treatment in a high percentage of patients, with this highly effective therapeutic agent. The WHO is setting up field demonstration units to acquaint physicians throughout the world with the use of penicillin in the treatment of syphilis and to teach newer methods of diagnosis and treatment in the other venereal infections. The demonstration team assigned to Himachal Pradesh with headquarters in Simla is the first such WHO unit in the field.

The hill tracts of this area are said to have the highest rate of venereal infection of all India. There are several customs, namely *rheet* and *polyandry*, which contribute to the venereal disease problem. Polyandry has been practised for a long time in an effort to avoid splitting of the land, through inheritance, into holdings which would be too small for profitable farming or to support a family. In the custom of *rheet*, if the woman desires to leave one husband for another, the one who takes her must pay an agreed sum of money to the first husband. The woman can make the change at will if the price is paid and cases of five or more changes are not infrequently seen. It is stated that both practices are on the decline, but the significance in the spread of venereal infection is evident. A further complicating factor in this area is the belief that self-cure can be obtained by passing the venereal infection on to another sexual partner.

The first step in a serious approach to attacking the problem in the area has been to make surveys of representative samples of population to determine the actual rate of prevalence of the various infections. In carrying out such surveys, it is necessary to depend upon the various serologic tests for syphilis such as the Kahn flocculation, Wassermann complement fixation, and others. It has recently been called to attention by Mahoney, Arnold and Levitan that in areas of Central America the standard serologic tests for syphilis give a high incidence of false positive reactions. This finding cannot be explained alone by malaria or other common causes of false positive reactions. It is anticipated that similar findings will be encountered in other parts of the world, including India where conditions are similar. In 1941, Pangborn of the New York State Laboratories isolated cardiolipin, the active principle of the heart extracts that have been used in constructing antigens for serologic tests for syphilis (Pangborn, 1941). Extensive studies

since that time, both in the United States, Europe and in Central America, have shown that the use of cardiolipin as an antigen in the serologic test for syphilis will reduce the proportion of false positive tests. At the same time some of the new techniques developed such as the VDRL slide test with cardiolipin (Harris *et al.*, 1946; Harris *et al.*, 1948; Stitt *et al.*, 1948) have been designed so as to minimize the equipment needed for performance, while the antigen and reagents needed can be furnished in a form which is stable even in the hot climates, and the reagents are easily prepared for use. The simplicity of some of the newer tests and the relatively small amount of equipment needed are of the highest importance when it is desired to furnish facilities for laboratory diagnosis of syphilis to hospitals and clinics whose personnel and finances are limited. As rapidly as possible the WHO demonstration teams will complete the comparative studies of the newer simpler tests and the standard tests (Wassermann, Kahn, etc.). The importance of the availability of simple, easily performed, inexpensive test methods, which will give a minimum of false positive reactions in areas where malaria and other diseases confuse the serodiagnosis of syphilis, is self-evident.

As the basis for therapy the team will use penicillin to demonstrate the ease and effectiveness with which syphilis can be treated. The newest development is the procaine salt of penicillin G in oil with 2 per cent aluminum monostearate. With one injection of 300,000 units of this preparation a therapeutically significant blood level of penicillin, 0.03 unit per cc., can be demonstrated in the great majority of patients for 96 to 144 hours (Arnold *et al.*, 1949; Boger and Flippin, 1949). The first studies on treatment of early syphilis with a single injection of 300,000 units of this preparation indicate a satisfactory clinical response. The public health implications of this development are highly significant. In considering mass therapy of syphilis two objectives are desirable: (a) the first is to find and to treat in any group the largest number possible of open, contagious syphilis so as to reduce the infectious reservoir and (b) the second objective is to treat syphilis in the early stage so as to prevent the development of the latter and crippling complications. Thus it is evident that with a therapy which is inexpensive, easily administered, and which requires no hospitalizations, it is possible to think in terms of ambulatory mass treatment at a low cost.

The rate of success in treatment can be reliably predicted on the basis of the time-dosage schedule of penicillin used. When a physician in private practice treats a patient he is interested in using the best treatment regardless of the cost so as to assure a favourable outcome for the individual. However, the worker

in the field of public health thinks in terms of giving the maximum of benefit to the largest number of people possible at the minimum of cost. In terms of treatment of syphilis this means that treatment must be planned so that the largest possible number of patients may be cured by the use of a given amount of penicillin. This concept is illustrated by the following example: Assume that 1,000 cc. of procaine penicillin with 2 per cent aluminum monostearate is available to a V.D. centre. The number of cured patients which can be obtained with this amount of drug used according to various schedules is shown below:

Schedule	Number treated	Per cent relapse	Number re-treated	Number cured
300,000 units—1 cc.	1,000	15-20	150-200	750-800
900,000 units—3 cc. in doses of 300,000 units each . .	333	5-10	16-33	300-317
1,500,000 units—5 cc. in 5 doses of 1 cc. 300,000 units each	200	2-5	4-10	190-196

The advantage of using the smaller dose schedule so as to secure the largest number possible of cured, non-infectious patients with a given amount of drug is self-evident. Those patients relapsing can be re-treated as needed by larger doses of penicillin and cured for, to date, small doses of penicillin have not been demonstrated to cause the development of penicillin-resistant strains.

As part of the treatment demonstration programme, treatment of pregnant women with the same penicillin will be carried on. By this time a significant series of syphilitic women has been treated in various centres prior to or during pregnancy, providing the effectiveness of treatment with penicillin alone by the birth of non-syphilitic infants, some of whom have already been followed up to three years of age (Cole *et al.*, 1949; Aron *et al.*, 1947; Goodwin and Moore, 1946).

Besides demonstration of treatment method and study of relative performance of tests for syphilis, the WHO team will work with the other venereal diseases. Specific treatment is now available—the sulfonamides provide specific therapy for chancroid and lymphogranuloma venereum; streptomycin has been found to offer a satisfactory cure for granuloma inguinale; penicillin has proven completely curative for gonorrhoeal urethritis and to date no true penicillin-resistant strain of gonococcus has been

observed *in vivo*. It is evident that the means are available to control venereal diseases by treatment. What is now needed is adequate public health facilities to utilize the known therapeutic tools along with other V.D. control elements.

The WHO and the Government of India have set up the centre in Himachal Pradesh to demonstrate what can be done by utilizing the newer techniques available. The WHO team will train physicians, serologists, nurses and laboratory technicians in the newer methods used elsewhere, and it is expected that as the centre grows and is taken over by the venereal disease

division of the Ministry of Health, it may become an important teaching, standardization and research centre for venereal disease for the Government of India.

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Indian Medical Gazette

JANUARY

THE BIRTH OF THE INDIAN REPUBLIC

And slowly answered Arthur from the barge :
'The old order changeth, yielding place to new,
And God fulfils himself in many ways
Lest one good custom should corrupt the world.'

MORTE D'ARTHUR, TENNYSON.

On the 26th of January 1950 occurred this memorable birth in a memorable way : no pains, no anaesthesia, not even a twilight sleep, quite unlike the birth of another great republic descending from the same kingdom some time ago. In this difference in the course of events of the accouchement the old order has also changed yielding place to a new procedure.

The birth is really the final stage of a metamorphosis : Two Reforms, the Dominion Status and the Republic. The pains, pangs and agonies of the previous stages were duly remembered in the two minutes' silence on the memorable day : They died so that we may live in honour.

The Republic remains a full member of the British Commonwealth of Nations. In this membership too the old order has changed yielding a new definition of kingship : symbolic Head of an Association of Free Nations.

The Republic has received blessings from the Head of the Association of Free Nations as well as good wishes of the Associates.

Medicine being international to the core is not likely to be affected by political changes although the department of the State dealing with certain aspects of it may alter certain policies. The effect on its principles and practice will be negligible. Thus was introduced the Western Allopathic Medicine in India under Eastern Rule, in the days of the Mughals.

It will be in keeping with the birth of the Republic if the non-official medical profession took more interest in the affairs of the profession and even assumed advisory powers which it has not so far possessed. That may alter materially the outlook of the medical men in the country : Medical practice is not a matter of securing posts under the State, in spite of the recent experiments elsewhere in the Commonwealth countries. The medical man might enquire why there is need of running after posts breathlessly when there is supposed to exist, all over the country, an urgent need for medical relief; why practitioners called quacks by some allopaths thrive and compete successfully with the allopaths; why minor differences between the

allopaths, qualified under the rules of the State, are magnified and none recognized at all among others; whether the present allopathic system (apart from surgery and a few very recent therapeutic agents) has ever found acceptance with the masses, and if not, why not; whether the allopathic teaching in the country has yet been based on the indigenous environment, taste, means, and even symptomatology and temperament; whether the Indian system of medicine based on observation going back into the mist of antiquity cannot be freed from encumbering encrustations of superstition and ignorance, and put on a sound footing like the country itself which sank into coma and remained no more than animate for so many centuries; whether the Western system of medicine in its infatuation for the laboratory is not in serious danger of divorcement from traditional medicine built up by the masters of medicine in Europe and elsewhere; whether a freed Indian medicine after including the essentials of the Western medicine will not still remain Indian; whether certain ambitious plans are not mere expensive pets of some specialists; and many more questions even more probing.

That the ancient Indian medicine can be put on a firm foundation that will take any modern superstructure is no more presumptuous than the reinstatement of Asoka's pillar and wheel. Our statesmen have accomplished the second and our medical men are quite capable of accomplishing the first. In fact they seem to be in a stronger position. While the statesmen in their struggle against their opposite numbers of the last regime have been helped not inconsiderably by world events, the medical men in prominent positions in the world of science have held their own against their opposite numbers of the last regime by merit alone. Given facilities they will do all that can be done and should be done.

Humanity makes the nearest approach to Deity in the alleviation of suffering. That function is the mission in life of medical men.

धर्मचक्रः प्रवर्तनीय

Dharmachakra pravartaneya.

Let the wheel of duty go into motion.

Medical News

BRITISH EXPEDITION'S SEARCH FOR MEDICINAL PLANT

BASIS FOR TREATMENT OF RHEUMATOID ARTHRITIS
(From Release No. B.F. 18 issued by British Information Services, New Delhi)

THE seeds of a plant vitally needed to increase the production of synthetic cortisone for treating rheumatoid arthritis are being collected by a special three-man

expedition from Britain now in Nigeria (West Africa). The party is made up of a medical expert of the British Medical Research Council, a botanist and a scientific officer, both from the famous horticultural centre at Kew.

The discovery of cortisone, which is an organic substance similar to one of the glandular secretions of the human body, was made two years ago in the United States and can only be produced at a very high cost. It has been found, however, that a substance called sarmentogemin reduced the process of obtaining a synthesis of cortisone. This substance can be obtained from a creeper known as *Strophanthus sarmentosus*. The expedition now in Nigeria is testing out other species of the genus *Strophanthus* to discover which will give the highest yield of sarmentogemin.

Strophanthus sarmentosus, which is a beautiful white trumpet-shaped flower, is not only found in a wild state in Africa but is also cultivated in Northern India and parts of South-East Asia.

When the expedition returns to Britain it is expected that a considerable step forward will be made towards the production of synthetic cortisone for medical research into the treatment of rheumatoid arthritis. It is even suggested in some quarters that when cortisone is available in sufficient quantity it will be used in helping to lengthen the span of human life. The British Medical Research Council, however, advises great caution in advancing the belief that cortisone has properties by which it might be regarded as the 'elixir of life'.

PROGRESS TOWARDS AN INTERNATIONAL PHARMACOPŒIA

[Excerpts from a recent radio talk by Dr. C. H. Hampshire (United Kingdom), Chairman of the W.H.O. Expert Committee on Unification of Pharmacopœias, which held its fifth session at Geneva from 26th September to 5th October. Published in W.H.O. Newsletter, No. 11, October 1949]

THE word *Pharmacopœia*, used almost exclusively in medical and pharmaceutical circles, may be unfamiliar to most members of the general public. It is derived from a Greek word meaning 'a drug' and at the present time denotes a book containing descriptions and standards for drugs. The practice of collecting together such information dates back to the Middle Ages in Europe, when descriptions of the drugs used in a hospital or by a college of physicians were collected together for the guidance of those responsible for preparing the drugs. . . .

You will see that the key-note is uniformity, so that each person requiring any medicine should have, on each occasion when it is taken or used, a supply of the same strength and quality. This principle of uniformity, as time has gone on, has extended to larger areas. The position now is that each civilized country in the world has a national pharmacopœia which ensures, according to the laws of that country, that the medicines supplied are always uniform and constant. . . .

Why it is Needed

The existence of national pharmacopœias in the several countries has given rise to various difficulties, which have led to a desire, on the part of those interested, for an International Pharmacopœia. Differences in national standards for widely-used materials constitute a source of danger to travellers who may need to have the same prescription dispensed in different countries. We must remember the medical science has enabled many persons to prolong their lives in useful activity by means of suitable drugs, whereas in former times they would not have continued to be active. The instance of insulin is outstanding. People who require

insulin in order to keep them in good health may have to travel, and it is essential that the drug which they use daily should always be obtainable in the same strength in whatever country they may happen to find themselves. Similarly with drugs for the control of heart diseases, if a drug of the correct strength is not available, time is lost in making it specially, or procuring it from a distance.

Uniformity in drugs is also of great importance in trade between countries and also in medical research, since the conclusions of doctors working to discover the best drug or the best forms of giving drugs may become valueless, if it is not known exactly to what strength of drug or type of drug those conclusions refer. The different national pharmacopœias may also give different names to the same drug. A single example will suffice to show how confusing this may be. One of the most important antimalaria drugs, paludrine, was discovered by a leading British establishment. It carries the official designation of Proguanil in England, Chlorguanide in the U.S.A., Chloriguanine in France, and at the same time, either as a common name or registered trademark, in these countries or elsewhere, it also goes under the names Biguanyl, Drinupal, Guanatol, Palusil, Tirian, M 4888, 3359 RP, etc.

These considerations are made more forceful by the present-day increase in foreign travel and the rapidity of movement from one country to another now made possible by the aeroplane.

International Agreement

Early in the present century an International Agreement for the unification of drugs was signed by a number of countries. This was revised in 1929 and went some way in the direction of unifying the national pharmacopœias. This agreement contained a clause calling on the League of Nations to provide an organization for extending the unification of pharmacopœias. The Health Organization of the League set up in 1937 a Technical Commission of Pharmacopœial Experts. This commission had made considerable progress when the work had to be interrupted in consequence of the Second World War. Some work was done however during the war by the members of the commission who were able to communicate with one another. . . .

In 1947 the Interim Commission of the World Health Organization decided that the work should be resumed and appointed an Expert Committee on the Unification of Pharmacopœias, consisting of seven members. This was confirmed when the World Health Organization was established and represents one way in which the organization strives to fulfil its first object—the attainment by all peoples of the highest possible level of health. This committee has worked continuously since that time and has met on five occasions in Geneva.

It is now approaching the completion of its work for a first volume of an International Pharmacopœia. This volume will contain descriptions and standards for some 200 drugs in general use which are ordered by doctors for their patients. These include drugs for the relief of pain, for producing sleep, for use against infection, the sulphonamide drugs, vitamins and many other materials used in medicine. There are other subjects which it has been necessary to defer for a second volume. The rapid advances in certain aspects of medical science make it difficult to lay down definite fixed standards at present for such drugs as penicillin and streptomycin.

The committee will in future give increasing attention to the subject of names in the effort to secure that standardized names are made available for use in all countries.

The International Pharmacopœia can, of course, have no legal force in any country until the responsible authority in that country has approved it. However, it will serve as a basis for countries engaged in preparing or revising their own pharmacopœias and will provide standard descriptions which can be immediately adopted.



VAUXHALL REHABILITATION CENTRE

His shoulder is dislocated and nerves in the arm and elbow are injured; but with the aid of special devices this employee of the Vauxhall Motor Works in Luton is able to do a full day's work as he recovers. These days many industrial concerns run special workshops and training shops for the rehabilitation of the disabled.

MATERNAL AND CHILD HEALTH

FUTURE DEVELOPMENT IN INDIA

(From Press Release SEA/PR/50-1, dated 2nd January, 1950, issued by W.H.O. Regional Office for S.E. Asia, New Delhi)

A COMPLETE blue-print for the co-ordination and development of public services for the care of mothers and children in India was given final approval this afternoon at the closing session of the Symposium on Maternal and Child Health convened by the World Health Organization in New Delhi in collaboration with the Government of India. The nine pages of detailed and practical recommendations drawn up during four days of arduous work by more than sixty doctors and health experts attending the Symposium from all over

India form, in the opinion of many delegates, the most important document on maternity and child health in this country since the Bhole Report. The recommendations cover the following subjects: Organization and administration; personnel training (for doctors, nurses, midwives and dais); statistics; research; legislation; health education and school health.

The Hon. Rajkumari Amrit Kaur, Minister of Health, took the chair at the closing session.

The recommendations stressed that the maternal and child health service is not a speciality but is a basic part of the community health service. It serves to focus attention on the most vulnerable section of the people and to provide the most strategic point for attacking ignorance, poverty and disease. The scope of maternal and child health services as laid down by the conference includes the health of the mother and

of the child from birth to adolescence at home, at school, at work, and in industry, as well as the care and rehabilitation of the handicapped and unwanted child.

The experts attending the Symposium were unanimous on the necessity of integration of preventive and curative aspects of medicine and of developing social medicine to improve the quality and efficiency of existing health services in the country.

A recurrent theme stressed alike in lectures and discussions was the supreme importance of nutrition, education, environmental hygiene (including housing and sanitation), and all the factors influencing the standard of living in the total frame of mother and child care. Active co-operation at every level is therefore recommended between departments of health, education, agriculture, social welfare, labour, etc., and between official and voluntary organizations. Projects in all these fields should, the conference agreed, be integrated.

One of the most progressive recommendations made by the Symposium is for the development of existing dispensaries and maternity and child welfare centres into comprehensive health centres providing care and treatment for the health needs of the whole family. A pioneer venture of this kind, it was learnt, is the Ashok Vihar in Madras.

All administrative officers should, it was further recommended, take more interest in the health and welfare of people particularly mothers and children in rural areas. To make service outside the towns more attractive, nine minimum conditions of employment for rural health workers were laid down, including a rural allowance of not less than 25 per cent of basic salary, free furnished accommodation, and special facilities for transport, children's education, etc.

Maternal and child health services should be strengthened, re-organized and energized at the centre, in the provinces and in the states, the experts agreed. More adequate equipment, supplies, and nursing, and other staff, for existing public health services, it was further agreed, should be provided to enable them to function more efficiently.

The public health nurse, it was emphasized, is the essential primary field worker both in rural and urban areas. Some of the most important recommendations dealt with facilities for obtaining basic and post-certificate nursing courses.

Concerning personnel training, the experts recommended that increased importance be given to field work in training personnel; that personnel in different branches should be trained together to promote the habit of team-work; that child care and the treatment of children's diseases should be given equal importance with other branches of training; and that mental health should be included in all medical and nursing courses. Standards of training for Prasava Sevikas (midwives) and for hereditary dais were also recommended by the Symposium.

During the four days' conference, lectures were given by experts on: Administration of maternal and child health programmes; nutrition of children; co-ordination of social and health services; care of infants and toddlers; common diseases of children; care of school-age child; and personnel needs and personnel preparation.

Among those attending the Symposium were: Dr. George Coelho, B. J. Hospital for Children, Bombay; Dr. K. C. Chaudhury, Medical College, Calcutta; Dr. Chinnappa, Indian Red Cross Society, New Delhi; Dr. (Mrs.) Soundaram Ramchandran, Gandhigram, Wardha; Dr. P. S. Sambandam, Director, Ashok Vihar, Madras; Dr. S. Pandit, Adviser to the Government of India in Maternity and Child Welfare; Dr. H. M. Lazarus, Principal, Women's Christian Medical College, Vellore; Mrs. Clubwala, Hony. Secretary, Guild of Service, Madras; Dr. Muktha Sen,

Professor, All-India Institute of Hygiene and Public Health, Calcutta.

AMENDMENTS TO DRUG RULES, 1945

No. F.1-30/47-D, Government of India, Ministry of Health, New Delhi, the 5th January, 1950

NOTIFICATION

IN exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drug Rules, 1945, the same having been previously published as required by the said sections, namely:—

In the said Rules:—

- (1) In Schedule C, for item 3, the following item shall be substituted, namely:—
'3. Vaccines for parenteral injections.'
- (2) In Schedule C(1), after item 7, the following item shall be added, namely:—
'8. Vaccines not in a form to be administered parenterally.'

(Sd.) J. N. SAKSENA,

Under Secretary.

INTERNATIONAL HONOUR FOR INDIAN SCIENTIST: Dr. ZAL R. KOTHAVALA

(From a Release issued by Press Information Bureau, Government of India, dated 26th December, 1949)

THE International Dairy Federation, recognized as the highest authoritative body on dairying in the world, has awarded a Silver Medal to Dr. Zal R. Kothavala, Dairy Development Adviser to the Government of India in the Ministry of Agriculture, for outstanding contribution to the science and practice of dairying. The award was made by the World Dairy Congress at its 12th meeting held at Stockholm in August last. This Medal is generally awarded to a person in a member country of the International Dairy Federation who has made an outstanding contribution to the science and practice of dairy towards the advancement of the cattle industry of the country.

Dr. Kothavala has also been awarded the 'Moos Medal' by the Bombay University for his scientific work on dairy husbandry on the thesis of which he has been awarded the Degree of D.Sc. by that university. This is the first time that a Degree of D.Sc. was awarded by any university in India for work on dairy husbandry in the tropics.

THE DR. B. S. SHROFF MEMORIAL GOLD MEDAL OF THE BOMBAY MEDICAL UNION, 1949

THE following subject has been selected by the Bombay Medical Union for competitive thesis for the above prize for 1949:

'Medical Problems met with in Textile Industrial Centres and Suggestions re: Promotion of Their Health.'

The award will be in the form of a Gold Medal called the DR. B. S. SHROFF MEMORIAL GOLD MEDAL OF THE BOMBAY MEDICAL UNION.

The competitor must be (i) a duly qualified member of the medical profession holding a degree or degrees

and diplomas from Indian and other universities created for statute, or (ii) a duly qualified member of the medical profession holding the diploma of membership of the College of Physicians and Surgeons of Bombay.

The thesis must be sent in three clear typed copies so as to reach the Honorary Secretaries, Bombay Medical Union, Blavatsky Lodge Building, French Bridge, Chowpaty, Bombay 7, by the 30th June, 1950.

The thesis should be designated by a motto instead of the writer's name and should be accompanied by a sealed cover containing the name of the writer and his Post Office address.

The name of the prize, the year of competition, the subject of the thesis, and the writer's motto should be superscribed on the cover.

No study or essay that has been published in the medical press or elsewhere will be considered eligible for the prize, and no contribution, offered in one year, will be accepted in any subsequent year unless it includes evidence of further work.

The accepted thesis shall be the property of the Bombay Medical Union.

All other theses shall be returned if not accepted provided the return postage expenses are paid in advance by the writer.

In the award of the prize to the successful candidate, the decision of the committee shall be final.

THE DR. SIR BHALCHANDRA KRISHNA, Kt., MEMORIAL GOLD MEDAL OF THE BOMBAY MEDICAL UNION, 1949

At a meeting of the subscribers of Sir Bhalechandra Krishna, Kt., Memorial Fund held on the 11th July, 1924, the following resolution was adopted :—

'That from the funds collected to perpetuate the memory of the late Dr. Sir Bhalechandra Krishna, Kt., a memorial prize medal be founded to be awarded every year on the anniversary of his death to a member of the medical profession* who submits a thesis or delivers a lecture on any medical subject before a meeting of the medical profession to be held under the auspices of the Bombay Medical Union, preference to be given to one who submits any original or research work especially with reference to indigenous medicine on Western lines.'

In consequence with the above resolution, members of the profession are invited to submit a thesis or a paper by the 30th June, 1950, to the undersigned for submission to a Selection Committee for making the above award.

The thesis should be designated by a motto instead of the writer's name and should be accompanied by a sealed cover containing the name of the writer and his Post Office address.

The name of the prize, the year of competition, the subject of the thesis and the writer's motto should be superscribed on the cover. Two or three copies of the thesis should be submitted.

The thesis or paper shall have to be read by the prizeman on the day of the award at a meeting of the profession to be held in accordance with the above resolution.

* A member of the medical profession means :—
All duly qualified members of the medical profession holding degrees and diplomas from :—

- (a) Indian universities created by statute; and
- (b) Such other universities and corporate bodies as the managing committee may from time to time determine subject to the approval of the general body of the union; and
- (c) Duly qualified members of the medical profession holding diplomas of membership of the College of Physicians and Surgeons of Bombay.

The Indian Medical Gazette Fifty Years Ago

THE CALCUTTA HEALTH OFFICER'S REPORT

(From the *Indian Medical Gazette*, 1900,
Vol. 35, p. 29)

THIS report is dated 30th June, 1899, but we have only recently received it. A report on the health of Calcutta without an account of the plague seems strange; but Dr. Neild Cook explains that the control of plague measures was in the hands of another officer who submitted a separate report (Major C. R. M. Green, I.M.S., F.R.C.S.). The Calcutta birth-rate is very low, only 13.9 per mille, but this is explained by the comparatively small number of women and the floating nature of the population. The death-rate is given at 29.8, the lowest since 1893, the mean decennial death-rate being 32.6. The year was a healthy one, due to the falling off in the number of deaths from cholera, small-pox and fevers. The couple of hundred deaths from plague did not materially influence the rate. The infantile mortality is in Calcutta appallingly high, 368 mille for 1898, with a five years' mean of 437. Dr. Cook writes: 'The infantile mortality of Calcutta must remain high, until the town is opened out and a higher standard of personal hygiene, including midwifery practice, is attained. It is further conducted to by the women in many cases working on a poor diet up to the time of confinement'. The mortality is further explained lower down in this report, where Dr. Cook shows the enormous extent to which milk is adulterated in Calcutta. Milk is adulterated with from 10 to 75 per cent of water, 30 per cent the average.

'It would be interesting to know', writes Dr. Cook, 'how many infant lives this simple-minded felon (the milkman) accounts for on the average in the year'.

The mortality from fevers was lower than usual. Dr. Cook is taking measures, in consultation with Major Roland Ross, to apply the mosquito theory to Calcutta malaria. It will be interesting to see the results, but till the question of re-infection or relapse is settled, it will be difficult to judge. Personally, we think, that a large amount of fever in natives of India is due to relapses; possibly if those who suffered from malarial fever took quinine regularly for two or three weeks after an attack, relapses would be few. But how few do so? There were 142 cases of small-pox during the year in Calcutta, 85 of which were fatal. The incidence was 27 per cent vaccinated (in childhood), 2.8 per cent inoculated, and 61 per cent unprotected. The mortality of the vaccinated cases was 44.9

per cent; 100 among the inoculated, and 63.0 per cent among the unprotected. Vaccination was much hindered during the part of the year owing to the plague inoculation scare. In Calcutta, on the average, about 1,000 deaths a year are registered from phthisis, about 800 cases of asthma, 700 cases of tetanus, and 1,440 cases of 'remittent fever'. How many fevers are embraced in this term remittent, it is impossible to say; only eight deaths in 1897 and in 1898 are registered from enteric fever! The vaccine lymph used in Calcutta is received from the Government animal vaccine depot. The 'rate of success per cent in ascertained cases' is given at 99.2, 99.2 and 100 per cent for calf, lanolin and humanized lymph respectively. This being so, we can only interpret 'ascertained cases' to mean that the failures were hid away. Dr. Cook has proposed an admirable scheme for the improvement of the Calcutta vaccination department.

The municipal laboratory did a large amount of work during the year in the bacteriological examination of cases of plague, enteric, etc., as well as numerous examinations of drinking water and analyses of foodstuff and adulterations. Dr. Cook concludes his interesting report by stating that 'nothing approaching an average standard of sanitation can be attained without, to a considerable extent, demolishing and reconstructing the town'. The proposal for the Central Railway station, if carried out, would be the first step in this direction.

Current Topics, Etc.

New Tool for the Kitchen

(Abstracted from the *Medical Press*, Vol. 221, 16th March, 1949, p. 261)

WE would draw attention to one of the latest developments in the culinary world, described as 'pressure cooking'.

Pressure cooking has several distinct and outstanding advantages which can readily be grasped if we examine the basis on which it is carried out. Instead of cooking in a pan of boiling water at ordinary atmospheric pressure, with the lid off, or suitably adjusted so as to allow the steam to escape, the pressure cooker has a gas-proof lid fitted with a valve. This valve is so designed that when the water boils the steam is retained until it reaches a pressure of some 15 pounds, at which point it escapes. This pressure of 15 pounds can be maintained by a very much smaller amount of fuel than is required for a cooker with an open lid, while at the same time the temperature reaches approximately 250°F. Steam at this temperature and pressure has a much higher penetrative power than steam at normal atmospheric pressure, the result being that the time required thoroughly to cook any given article of food is reduced, frequently by as much as 75 per cent. Coupling this fact with the reduced amount of fuel required to maintain temperature in a cooker of efficient design, it is obvious that the widespread adop-

tion of pressure cooking would, if it did nothing else, lead to a tremendous saving of the fuel required for domestic consumption. This alone is a matter of national importance.

But, of course, saving in time and fuel, admirable though it is, can be of minor interest to the nutritionist whose main concern is with the nutritive value of the food so prepared. And on this point it is interesting to note that there seems to be a general consensus of mis-informed opinion that pressure-cooked food is inherently inferior to food cooked in the traditional fashion. In fact, this impression is quite erroneous.

The average modern pressure cooker requires little more than about a quarter-pint of water. The conservation of vitamin C and B₁ is greater than by ordinary methods, according to Yudkin, while we have the authority of the Ministry of Food for the statement that vitamins A and D are not adversely affected by the concentrated heat of pressure cooking. The vitamin content of those vegetables commonly employed in the ordinary household to supply bulk and protein supplements, namely, potatoes and the pulses, shows a pronounced improvement in conservation by pressure cooking. Potatoes, for instance, show a 25 per cent increase in the vitamin C, while the pulses—peas, beans and lentils—demonstrate that anything from 17 to 67 per cent more vitamin B₁ may be conserved than when they are boiled in the ordinary manner. The content of such minerals as calcium and phosphorus also compares favourably with that of vegetables cooked in the traditional manner, while the colour, texture and, above all, the flavour, are considerably enhanced.

Pressure cooking would seem to have an important bearing, not only on our domestic economy, but on hospital cooking as well, and it must have a particular interest for all those concerned with the diets of invalids and infants. Except in the case of soups and stews, vegetables are kept out of water and at the same time protected from the air, hence the superiority in flavour and the retention of colour. Furthermore, since the cooking time is short there is little or no temptation to curtail it, so that under-cooking is rare; cellulose can be quite disintegrated and starch grains thoroughly cooked with a consequent gain in digestibility. As for meat, the most unpromising pemmican may be reduced to abject tenderness. Indeed, by this means even the very bones themselves can be compelled to yield some 25 per cent of their weight in marrow fat, a foodstuff of high nutritional value in itself, while the resultant stock comprises a foundation food for invalids and children that is not to be despised, especially when it is known that its calcium content is unusually high.

Folic Acid Incompatibilities

(From the *Pharmaceutical Journal*, Vol. 162, 18th June, 1949, p. 458)

THE stability of folic acid in mixtures has been investigated by Scheindein (*Amer. J. Pharm.*, 1948, **120**, 103). As a result of his observations, he recommends that folic acid should not be dispensed with any of the following: Phenobarbitone, chloral hydrate, quinine dihydrochloride, tinctures of hyoscyamus, stramonium, nux vomica or digitalis. It was found that sulphadiazine rapidly destroyed the activity of folic acid.

Travel Sickness

(From the *Medical Review*, Vol. 43, June 1949, p. 81)

THE maintenance of equilibrium is a vital necessity, and travel or motion sickness is an expression of the disturbance of equilibrium. Symptoms may be experienced under a wide variety of circumstances, such as swinging, travelling in a car, train, ship or air-plane.

They may be aggravated by such physical factors as poor ventilation, unpleasant odours, and by psychological factors (the sight of others being seasick). Constipation is thought to act as a predisposing factor. Although the exact mechanism of motion sickness, and the nerve paths involved, is not clearly understood, it is thought that stimulation of the labyrinth and over-activity of the vagus nerve are the two chief factors. The symptoms are chiefly headache, loss of appetite, nausea, and vomiting. They may be accompanied by diarrhoea, but more often by constipation. In severe cases there may be vertigo and almost continuous vomiting. Bayer Products Ltd. market a brand of travel-sickness remedy under their trade mark 'T.S.R.'.

The formula of 'T.S.R.' is based upon war-time research and experience in the prevention of sickness from sea, air, train and other forms of travel and motion. This experience showed quite clearly that the best available single drug was scopolamine (hyoscine); and, in combination with atropine and a barbiturate, it was used extensively by the United States armed forces. Such a combination is now available in 'T.S.R.' and, prior to general release in this country, the preparation was subjected during the winter months to large-scale clinical trials in collaboration with a well-known British passenger-carrying steamship company. The results showed it to be the most efficient means of preventing seasickness as yet available.

Each tablet contains: Scopolamine hydrobromide, 1/300 gr., atropine sulphate, 1/400 gr., and luminal (brand of phenobarbitone), 1/2 gr.

Action of 'T.S.R.'—'T.S.R.' contains the major belladonna alkaloids, scopolamine, and atropine, which have two principal actions in the body: (1) on the central nervous system, and (2) on smooth muscle and on secretory glands innervated by post-ganglionic parasympathetic nerves.

Atropine produces stimulation of the medulla and higher cerebral centres. Some increase in rate and occasionally the depth of respiration may be expected.

Scopolamine is primarily a depressant, having a sedative effect, and normally causing drowsiness, fatigue and dreamless sleep. Occasionally excitement and restlessness are encountered. The addition of luminal in 'T.S.R.' provides a further sedative action.

The belladonna alkaloids affect both the secretory and motor activities of the gastro-intestinal tract and the salivary secretions are inhibited. On the whole, the normal gastric secretion is not significantly altered by these drugs. The psychic phase of secretion, mediated by the vagus, is reduced but not abolished. The chemical phase of gastric secretion is not greatly altered by atropine; volume may be reduced slightly, but acidity is not lowered. The duration of the effects on gastric secretion is brief compared with that on the salivary glands. Atropine does not markedly affect the gastric evacuation time in normal subjects, but when the stomach is excessively motile and hypertonic the drug abolishes hyperactivity and restores normal peristaltic rhythm.

Administration and dosage.—'T.S.R.' may be administered before, at the start of travel, and during travel. The usual procedure is to prescribe for an adult one tablet thirty minutes before boarding the ship, plane, train or automobile. A second tablet is administered at the time of embarkation. The dose (one tablet) may be repeated at three- or four-hourly intervals, with a maximum of four tablets per day. Occasionally in severe conditions, two tablets are given on embarkation, but the dosage should be kept as low as possible. Children should receive half a tablet as above.

By-effects.—The dangers of idiosyncrasy to the components of 'T.S.R.' and of overdosage should be borne in mind. Caution is particularly indicated in prescribing 'T.S.R.' to pilots or automobile drivers, since the preparation may cause drowsiness or temporary visual disturbance, i.e. failure to accommodate.

Packings.—Tablets, individually sealed in cellulose film, in packings of 10 and 50.

Oral Reactions to Penicillin

By W. G. CROSS

(From the *Brit. Med. Jour.*, i, 29th January, 1949, p. 171, as abstracted in the *Acta Medica Orientalia*, Vol. 8, January-February 1949, p. 31)

THE author presents a review of cases of oral reactions to penicillin used locally in the mouth. Neither nicotinamide deficiency nor the lozenge base is responsible for these oral reactions. A total of 59 cases of oral reactions to penicillin have been studied. The two common conditions are discoloration of the tongue and stomatitis, in the latter condition glossitis being marked. In many cases the mouth cavity, as tested by the salivary count, was either sterile or contained coliform organisms. In a number of cases, however, other pathogenic bacteria were present. It was noticed that reactions do not occur until there has been a complete change in the character of the oral flora. This takes about 48 hours and it seems reasonable to limit the use of penicillin for the treatment of oral infections to this length of time as a rule. To maintain an adequate and continuous concentration of penicillin in the mouth, the use of this antibiotic in chewing-gum, 10,000 units per piece, thrice daily is suggested.

The Excretion of Penicillin in Human Milk

By R. ROZANSKY
and
A. BRZEZINSKY

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 34, April 1949, p. 497)

A study was made on the penicillin concentration in milk of thirteen women after intramuscular administration of the drug. Significant quantities of penicillin were found in the milk of twelve of these subjects.

Penicillin was found in milk one hour after the injection. Up to four hours after the injection the level rose, followed by a gradual fall in the concentration.

In two of the three subjects examined, penicillin was still found nine hours after the injection.

The Problem of Weakness and Fatigue

By M. Y. SILVER

(Abstracted from the *American Practitioner*, Vol. 3, June 1949, p. 598)

ONE of the most common problems facing the practitioner is the diagnosis and treatment of weakness and fatigue. Despite the relative frequency with which these symptoms occur, they are all too frequently misdiagnosed. A diagnosis of hypotension, hypothyroidism, anaemia, vitamin-deficiency state or menopausal syndrome is made in the absence of supporting evidence. The use of drugs to raise the blood pressure, to increase the metabolic rate or to supplement the iron and vitamin intake may make the patient feel better because of their suggestive value. The patient's symptoms are attributed to a diseased state and the responsibility for the patient's improvement falls entirely on the physician rather than on the patient. Unfortunately, too many times the problem is largely functional and the neurotic tendencies of the patient are fostered rather than treated. Although suggestion has a place in the management of these conditions, it is probably not the treatment of choice.

In fatigue states, as in any diagnostic problem, we are confronted with the difficulty of evaluating the organic and functional components of the patient's illness. In a series of three hundred cases presenting weakness or fatigue as the chief complaint at the Lahey Clinic, F. N. Allen found that only 20 per cent were associated with an organic aetiology of sufficient extent to explain the symptoms. Malignancy states, acute and chronic infections (*i.e.* tuberculosis), diabetes, heart disease, pronounced anaemia, severe liver and kidney disease and various neurologic disorders (*i.e.* myasthenia gravis) are common physical causes of fatigue. Recovery from the organic illness is generally followed by return to normal vigour and sense of well-being. In a small proportion of cases, the fatigue may persist, which should lead the physician to re-evaluate the functional problem. Having satisfied ourselves as to the absence of carcinoma or other acute or chronic debilitating disease, we are then in a better position to concentrate the functional problem.

THE MOST COMMON CAUSE

The great majority of patients complaining of fatigue have a functional illness. Many of these patients are suffering from anxiety states. Some of them sleep poorly at night and when they do sleep, they are not deeply asleep. The source of their anxiety prevents complete mental and physical relaxation at night. Frequently patients will tell you that they get from 8 to 10 hours of sleep at night and are still tired when they wake up in the morning. Here again one must evaluate the depth of sleep the night before. The presence of dreams at night usually indicates light sleep.

Many patients who complain of fatigue are mildly or seriously depressed. Some are frustrated by an intolerable life situation. Loss of appetite, insomnia, impairment in power of concentration and memory and a feeling of depression are often concomitant symptoms. When these symptoms are absent, a depression may not be obvious.

There still remains a large number of patients who do not seem to fit into clear-cut anxiety or depression states or combinations of these. Many of these people have become accustomed to a certain routine of living and its pattern has become so stereotyped that they have nothing special to look forward to from day to day. They are bored with life. Things that seemed important at one period of life have lost their attraction. With nothing special to look forward to each day, 'lying around' becomes a habit and there is not sufficient incentive after a while for the individual to overcome the inertia of rest. Fatigue states occur more often in women than in men because of the more routine nature of their daily responsibilities.

Fatigue is, to some extent, a disease of civilization. In certain communities afternoon rest periods are part of the programme for the day. Fatigue, or the desire for rest, is not a disease but an accepted part of daily living. The American businessman who rushes every day and lives in a competitive world feels that he is suffering from some sort of disease or illness if he feels let down for even a short period of time. The expenditure of nervous energy is really a form of physical exhaustion because the tonus of the muscles is increased by nervous tension.

If we are convinced that no serious disease is responsible for the patient's fatigue, or if we have reason to believe that psychogenic factors are the most important thing that we are dealing with, psychotherapy is the treatment of choice. Patients with anxiety states of short duration may be helped by delving into the sources of their anxiety, if this is not too deeply seated. Mild sedatives at night may be necessary to help manage nocturnal restlessness. Care should be exercised not to oversedate the patient, as a hangover effect the following morning may make the fatigue state worse. Patients who suffer from a mild depression are frequently helped by Dexedrine at

breakfast and lunch. This frequently is a very valuable central nervous system stimulant. In the patient in whom fatigue occurs because of a routine habit of living, recreational outlets or new interests are frequently all that are needed, provided that the patient is sufficiently interested and has the incentive to undertake new activities.

More can be done for the fatigue patient by conversation than by drugs and gadgets.

Reviews

SKIN DISEASES IN GENERAL PRACTICE.—By F. Ray Bettley, T.D., M.D., F.R.C.P. 1949. Published by Eyre and Spottiswoode (Publishers) Ltd., 15, Bedford Street, Strand, W.C.2, London, on behalf of the practitioner. Pp. 260 plus illustrations. Price, 21s.

THE author has given to the general practitioner complete descriptions and treatments of eczema, occupational dermatoses, seborrhoeic dermatitis, psoriasis, impetigo, some fungus infections, rosacea, perineal pruritus, alopecia areata, some parasitic diseases, naevi and epithelial tumour of the skin. The diseases constitute over 80 per cent of his practice. An appendix gives full information on preparations used in skin practice and on concentration of substances used in patch-tests.

The get-up is good and price reasonable.

S. D. K. G.

A SYNOPSIS OF OBSTETRICS AND GYNÆCOLOGY.—By Aleck W. Bourne, M.A., M.B., B.Ch., F.R.C.S. Tenth Edition. Published by John Wright and Sons Ltd., Medical Publishers, 42/44, Triangle West, Bristol, London. 4 × 7½ in. Pp. 530 plus 167 illustrations. Price, 21s.

BETWEEN the first and present edition have passed 36 years during which the book has gained and retained its high reputation as a concise and safe guide to practical obstetrics and gynaecology.

The diagrams are characteristically simple and extremely instructive. One of them (figure 135) gives in a quarter of a page sites of gonorrhoea and is the best of its kind known to the reviewer.

The present addition gives the latest information on the latest therapeutic agents like penicillin and the latest aetiological factors like Rh.

The size has been kept constant by removing some items no longer required, like blood grouping.

The get-up is good and price reasonable.

S. D. K. G.

DISEASES OF WOMEN.—By Ten Teachers, C. White, F. Cook, Sir William Gillillatt and others. Eighth Edition. Messrs. Edward Arnold and Co., 41, Maddox Street, London, W.1. Pp. 461 plus illustration. Price, 25s.

ORIGINALLY written and edited under the late Sir Conynus Berkeley, this record of British wisdom on the subject has been revised and brought up to date now after seven years. It is a complete textbook beginning with the anatomy of the female pelvic organ.

Physiological action of the endocrine gland and of the menstrual function is given in accordance with the latest discoveries. Diseases, including venereal diseases, tumours and disorders of functions are covered with a directness characteristic of collaboration. So are the treatment and operative techniques. Illustrations are excellent. Contraception and sterilization have been included.

From the teachers to the pupils an excellent gift at a reasonable price.

S. D. K. G.

PRINCIPLES OF HUMAN PHYSIOLOGY (STARLING).—By C. Lovatt Evans, D.Sc., F.R.C.P., F.R.S., LL.D. Tenth Edition. J. and A. Churchill Ltd., 104, Gloucester Place, London, W.1. Pp. 1193 with 693 illustrations. Price, 42s.

This standard book of physiology is familiar to students, and needs no introduction. It is sufficient to say that it provides a sound foundation for knowledge of physiology and its clinical applications. Professor Lovatt Evans has incorporated many new features representing current trends and established advances. The book has slightly increased in size, this is partly due to the inclusion of 60 new figures.

R. N. C.

BOOKS RECEIVED

1. Annual Report of the Federal Security Agency, 1948. Public Health Service. United States Government Printing Office, Washington, 1949.
2. Indian Medical Guide: A Monthly Magazine devoted to Medicine, Surgery and Public Health. Editor Dr. Hoi Ardeshir Choksey, M.A.C.B., M.C.S. Vol. 11, No. 9, September 1949. Published by Thos. Peters at 231, Hornby Road, Bombay. Annual subscription Rs. 10.
3. Chronicle of the World Health Organization. Vol. 3, No. 5, May 1949.
4. Chronicle of the World Health Organization. Vol. 3, No. 6, June 1949.
5. Health Horizon, July 1949. Editor Harley Williams, M.D. Published by the National Association for the Prevention of Tuberculosis, Tavistock House, Tavistock Square, London, W.C.1, England. Pages 60 with illustrations. Quarterly: One and sixpence.
6. Enquiry: A Journal of Modern Thought. Vol. 2, No. 1, July 1949. Published for the Proprietors by Horace Cox Ltd., 239/241, Shaftesbury Avenue, London, W.C.2, Temple Bar. 3914/5. Subscription rates, including postage, for twelve issues: Inland 16s; Abroad 20s.
7. Nutritional Data (formerly 'Nutritional Charts'). Compiled by Harold A. Wooster, Jr., and Fred C. Blank (Mellon Institute, Pittsburgh). Published by H. J. Heinz Company, Pittsburgh, Penn. U.S.A. First Edition, 1949. 120 pages, plastic-bound. Gratis.
8. International Committee of the Red Cross, Geneva Medical Division. No. 5, August 1949. Health Conditions Among the Civilian Populations of Certain Countries Affected by the War.
9. Bulletin on Narcotics, No. 1, October 1949. United Nations Department of Social Affairs, Lake Success, New York.

Abstracts from Reports

ANNUAL REPORT OF THE CHEMICAL EXAMINER'S DEPARTMENT FOR THE YEAR 1948. PRINTED BY THE SUPERINTENDENT, GOVERNMENT PRESS, MADRAS. 1949. PRICE 4 AS. Pp. 10 PLUS 2

The vast majority of the poisons were organic poisons. The commonest poisons detected were opium in 68 cases, oleander in 39 cases and datura in 37 cases.

During the year 25 cases of animal poisoning were received compared with 28 cases in 1947. Poison was detected in 14 cases or 56 per cent of which arsenic was the commonest.

One thousand and eleven stain cases were examined in 1948 as against 991 cases in 1947. Nine hundred and eighteen cases were examined for blood and 93 cases for semen with or without blood. The total number of articles examined under these headings was 5,318. In 918 cases examined for blood, it was detected in 818 cases or 92.4 per cent. In 93 cases examined for

semen with or without blood the detections were semen in 25 cases, blood and semen in 7 cases, blood alone in 15 cases, and blood and saliva in one case, the total detections being 48 cases or 51.6 per cent.

Sixteen pieces of hair found sticking to weapons in blood stain cases were studied. Fifteen were found to be human hair and one to be goat's wool.

The report gives accounts of selected cases of medicinal interest. Dr. P. Venkat Rao was in charge of the department.

Correspondence

TREATMENT OF MALARIA

SIR,—I have read the questions column of the July issue of the *Indian Medical Gazette* for treatment of malaria with interest.

I am using as a routine quinine mixture (10 grains of quinine sulphate in 3 oz. of water per day) or quinarsol (Cipla) one tablet twice a day for the first two days along with the regular course of paludrine tablets, viz, 0.3 gm. twice a day for 10 days.

The action of paludrine is slow and the action of quinine is rapid and with this idea I started this treatment.

Before the doses of paludrine were revised, I used to give the same mixture or tablets along with paludrine 0.1 gm. three times a day for 10 days.

With this treatment the fever is controlled quickly and it is very rarely necessary to resort to injections of quinine bishydrochloride.

I had no case in which there was any complication with this treatment. I should like to know the experiences of others and appreciate your comments on the same.

Yours faithfully,

N. R. DANI, M.A., B.S., B.M.S.,
Medical Officer, Kapadwanj.

MUNICIPAL DISPENSARY,
16th December, 1949.

TYPHUS IN THE NORTHERN CIRCARS

SIR,—With reference to the article 'Typhus in the Northern Circars' that appeared in the *I.M.G.* for September 1949 (page 393) I may please be allowed to put forth my views about it.

While one agrees that some, if not many, of the pyrexias of unknown origin may be typhus-like or typhus fevers, it is not very safe to diagnose a case of typhus clinically especially when it relates to a couple of stray cases. In an epidemic, a case of clinical typhus, even with a negative Weil-Felix, would easily fit in. The same may be said of an endemic area.

I am of the opinion that a rise in titre should be taken as a diagnostic significance rather than depending upon one reading. In case 1, the titre might have gone higher either in X2 or X19 if it were repeated. Or it is possible it might be an anamnestic reaction and on subsequent tests the X2 and X19 might give negative result with gradual rise in XK titre. Very often the titre may begin to rise during convalescence. Therefore one negative reading during febrile period may put the physician on the wrong path.

The difficulty lies in clinching the diagnosis in such cases especially in areas where such cases are scarce. By clinching the diagnosis I do not mean that inoculation tests or specific agglutination tests (facilities for which are not available everywhere) should be done.

I would very much like to know the views of the readers.

Yours faithfully,

G. S. RAO, M.B., B.S.

SALUR,
27th December, 1949.

MEDICAL CORRESPONDENCE COLLEGE

SIR,—Reference your letter published in the *Indian Medical Gazette*, 84, No. 9, September 1949 issue, page 229, I agree with the view that experienced and expert Licentiates should be allowed to sit for M.B.B.S. Examination after a Clinical Training and College Attendance for six months only.

Medical Correspondence Colleges may be opened at Calcutta, Madras, Bombay, etc., to train up Licentiates of more than five years' standing by experienced professors who can give lessons by post and after satisfactory completion of such postal training candidates be allowed to take M.B.B.S. Examination after six months of further practical training in any recognized Medical College.

Such Medical Correspondence Colleges can fruitfully help in achieving the desired results by rendering uniform medical relief by basic doctors all over the country.

Yours faithfully,

K. N. DUTTA,

Radiologist, Ripon Hospital, Simla,
and President, A.I.M.L.A.,
Simla Branch.

SIMLA,

20th December, 1949.

COMBINATION OF LIVER EXTRACT AND FOLIC ACID

SIR,—I notice with interest the references on 'Combination of Liver Extract and Folic Acid' of Mr. F. W. Van Kalaveren, published in October 1949 issue of the *Gazette* and the answers from R. N. C.

The question was originally raised on the basis of a pointer in the 'Current Therapy', 1949. This appeared to be very significant in view of the prevailing tendency to combine anti-anæmic substances irrespective of a consideration of rationality and/or therapeutic efficacy. The references of your correspondent are interesting and apparently have been drawn from a different angle. There is another side of the picture that cannot possibly be ignored. The combination has been disfavoured from the point of view of rationale and clinical response. To support, I quote below a few lines from a communication to me by the commentator in the 'Current Therapy' Dr. Frank H. Bethell, Professor of Internal Medicine and Assistant Director, Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan, Ann Arbor, Michigan (U.S.A.).

'Folic acid is a relatively simple chemical compound ordinarily quite well absorbed from the gastro-intestinal tract. A large percentage of orally administered folic acid is excreted in the urine in twenty-four hours. Except in the presence of intestinal abnormalities, the oral dose of folic acid is essentially equivalent to the parenteral dose. On the other hand, liver extract is a complex mixture and we believe that so far as pernicious anæmia is concerned, the active substance in the liver is vitamin B₁₂. This is a compound of high molecular weight and apparently is excreted very slowly, even after parenteral administration. In cases of pernicious anæmia the effective oral dose is from 50 to 100 times the parenteral dose. In the few instances where we believe the administration of both folic acid and vitamin B₁₂, or liver extract, are indicated, we have followed a plan of daily oral administration of folic acid, usually in a dosage of 5 mg., and we have given liver extract, or vitamin B₁₂, parenterally at intervals of one to three weeks. From the standpoint of clinical efficacy as well as scientific rationale, it therefore appears illogical to employ combinations of folic acid and liver extract, or vitamin B₁₂, in either oral or parenteral preparations.'

As regards administration of folic acid in pernicious anæmia, R. N. C. has rightly pointed out that its use is not indicated. To cite for instance, Jacobson *et al.* (*Jl. of the Amer. Med. Assoc.*, Vol. 137, No. 10, 3rd

July, 1948) refer two cases of Addisonian pernicious anæmia treated with folic acid. In these cases though an initial encouraging response was obtained, neurologic exacerbations developed. Spies, Vilter, C. F., and Vilter, R. W. (*J. Lab. and Clin. Med.*, Vol. 32, pages 262 and 1426, 1947) observed that folic (pteroylglutamic) acid will not control the neurologic symptoms as liver extract in pernicious anæmia. A still more conclusive finding has been referred in a leading article on 'Treatment of Pernicious Anæmia' in the *Lancet* (3rd December, 1949, p. 1041). 'Folic acid preparations—these should not be used for the treatment of pernicious anæmia. The reason, which we have noticed before, is that folic acid will not prevent neurological complications and may even accelerate their appearance; patients who have initially no disease of the central nervous system develop it if kept on folic acid for long; a recent estimate puts the risk at 80 per cent. Administration of folic acid is the correct treatment for some megaloblastic anæmias—notably sprue—but not for pernicious anæmia.....' The position is then, that despite much agitation and promise of later advances, the treatment of pernicious anæmia, to-day, still rests on proper use of liver and desiccated-stomach preparations.'

Combination of liver extract and folic acid appears to have so long been fostered on premature trials and reports. The foregoing references and the comments of R. N. C. relate certain facts for what they are worth and I see no reason why they should not be accepted.

Yours faithfully,

A. C. DEY, L.M.F.,

Head of the Scientific and
Propaganda Department.

UNION DRUG CO., LTD.,
CALCUTTA 12.

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CONTENTS

	Page		Page
ORIGINAL ARTICLES		EDITORIALS	
Chloroquine in the Treatment of Amoebic Liver Abscess. <i>By Chamlong Harnasuta, M.B. (Chula.), D.T.M. (Cal)</i> ..	37	Pleasant 1949-50 Winter in Calcutta and Associated Considerations ..	59
Intensified Electrical Convulsive Therapy in a Military Hospital. <i>By Kirpal Singh, Major, I.A.M.C.</i> ..	41	Index for Volume 84, 1949 ..	66
Studies on Sex Hormones. Part I. Sperm test of pregnancy utilizing male toad, <i>Bufo melanostictus</i> Schneid., as test animal. <i>By J. K. Mohanty, M.B., B.S., and Paramjit R. Pabrai, M.Pharm.</i> ..	43	ERRATUM ..	66
Incidence of Arthritis in Smallpox. <i>By R. N. Chatterjee, M.B., B.M.S.</i> ..	49	SPECIAL ARTICLE	
Studies on Arsenoxide Derivatives. Part I. Toxicity of carbamidophenyl-arsenious acid in comparison with carbarsonne. <i>By A. N. Bose, M.B., Sripati Bose, M.Sc., and T. N. Ghosh, D.Sc.</i> ..	50	Mammary Carcinoma. <i>By P. N. Ray, M.B., F.R.C.S. (Eng.)</i> ..	66
A MIRROR OF HOSPITAL PRACTICE		MEDICAL NEWS	
Two Cases of Vesicular (Weeping) Eczema treated with Anti-histaminic Drug. <i>By P. C. Sen, L.M.P.</i> ..	54	SCIENCE IN AID OF HUMAN WELFARE. FIRST NATIONAL LABORATORY TO BE OPENED. A VISION REALIZED ..	68
OCCASIONAL NOTES		PLAGUE. <i>By Georges Blanc</i> ..	69
The Place of Clinical Pathological Museum in Medical Education. <i>By P. N. Wahi, M.D., M.R.C.P. (Lond.), and K. C. Samuel, M.B., B.S.</i> ..	54	9TH BENGAL PROVINCIAL MEDICAL CONFERENCE ..	69
THERAPEUTIC NOTES		DRUG RULES, 1945 ..	70
Notes on Some Remedies. XXXII. Dehydration and its treatment. <i>By R. N. Chaudhuri, M.B., M.R.C.P., T.D.D.</i> ..	57	ASSOCIATION OF PHYSICIANS OF INDIA ..	70
		THE 16TH ANDHRA PROVINCIAL MEDICAL CONFERENCE ..	70
		INDIAN SCIENTIST ACCEPTS HIGH POST IN W.H.O. ..	70
		MEETING MEDICAL PROFESSION'S NEED OF DRUGS AND SURGICAL INSTRUMENTS: MORE LIBERAL IMPORT POLICY ..	71
		W.H.O. EXECUTIVE MEETS IN GENEVA ..	71
		W.H.O. EXPERTS ON DRUG ADDICTION MEET TO ADVISE U.N. ..	72
		ACCIDENT PREVENTION IN FACTORIES. HOW BRITAIN SAFEGUARDS WORKERS' HEALTH. <i>By S. Gordon Coller</i> ..	72

(Continued on page 36)

CONTENTS—(Continued from page 35)

	Page		Page
DELHI TO HOUSE ONE OF ASIA'S LARGEST AND MOST MODERN SCIENTIFIC INSTITUTIONS	73	SYNOPSIS OF PSYCHOSOMATIC DIAGNOSIS AND TREATMENT. <i>By Flanders Dunbar, M.D., et al.</i> 1948	81
PUBLIC HEALTH SECTION		THE AMERICAN NURSES' DICTIONARY. THE DEFINITION AND PRONUNCIATION OF TERMS IN THE NURSING VOCABULARY. <i>By A. L. Price, B.S., R.N.</i> 1949	81
Protective Value of BCG Vaccination ..	74	CLINICAL LABORATORY METHODS AND DIAGNOSIS. <i>By R. B. H. Gradwohl. Fourth Edition.</i> 1948	82
FIFTY YEARS AGO		TRENDS IN NURSING HISTORY. THEIR RELATIONSHIP TO WORLD EVENTS. <i>By E. M. Jamieson, B.A., R.N., and Mary F. Sewell, B.S., R.N. Third Edition.</i> 1949	82
ORGANIZATIONS FOR RESEARCH (<i>Indian Medical Gazette</i> , February 1900, Vol. 35, p. 63)	77	BOOKS RECEIVED .. 82	
CURRENT TOPICS, ETC.		ABSTRACTS FROM REPORTS	
PHYSICAL TREATMENT OF THE HÆMIPLEGIC PATIENT IN GENERAL PRACTICE. <i>By H. Dinken (Journal of the American Medical Association</i> , Vol. 139, 30th April, 1949, p. 1255)	79	ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, TOGETHER WITH THE FORTY-SECOND ANNUAL REPORT OF THE CENTRAL COMMITTEE OF THE PASTEUR INSTITUTE ASSOCIATION, 1948-49, MADRAS, PRINTED AT DIOCESAN PRESS, 1949	83
PARA-AMINOSALICYLIC ACID (P.A.S.) IN PULMONARY TUBERCULOSIS. <i>By M. M. Nagley and M. H. Logg (Lancet</i> , i, 28th May, 1949, p. 913)	79	DRUG STANDARDIZATION IN INDIA : REPORT OF THE GOVERNMENT LABORATORY	83
HICCUP (<i>Lancet</i> , i, 14th May, 1949, p. 830) ..	80	CORRESPONDENCE	
ABSORBABLE HÆMOSTATICS (<i>British Medical Journal</i> , i, 11th June, 1949, p. 1044) ..	80	WASSERMANN REACTION	84
REVIEWS		UNUSUAL CURE OF ANGINA PECTORIS AFTER VIRUS DISEASE	84
HUMAN BIOCHEMISTRY. <i>By Israel S. Kleiner, Ph.D. Second Edition.</i> 1948 ..	81	SERVICE NOTES .. 84	
NUTRITION. <i>By Lieut.-Colonel Barkat Narain. Second Edition</i>	81		
RADIOTHERAPY AND CANCER. <i>By A. G. C. Taylor, M.R.C.S., L.R.C.P., D.R., F.F.R., J. Lassetter, M.B., Ch.B., D.R., and T. K. Morgan, M.B., M.R.C.S., D.M.R.(T.).</i> 1948	81		

Original Articles

CHLOROQUINE IN THE TREATMENT OF AMÆBIC LIVER ABSCESS*

By CHAMLONG HARINASUTA, M.B. (Chula.),
D.T.M. (Cal.)

CHLOROQUINE, known in America as Aralen, has recently been introduced as a highly effective and well-tolerated antimalarial, following extensive laboratory and clinical experimentation. Subsequently it was shown that *in vitro* this substance had an amœbicidal activity superior to that of carbarsone and of anayodin (Yatren), although inferior to that of emetine. Conan (1948, 1949) found clinically that chloroquine effected symptomatic and parasitic cure in seventeen out of thirty-two cases of intestinal amœbiasis and yielded radical cure in all of seven cases of amœbic hepatitis. The latter result was confirmed by Shookhoff (Conan, 1949) and by Sodeman (Conan, 1949). Murgatroyd and Kent (1948) reported the cure of a draining amœbic abscess of the liver. Manson-Bahr (1949) described one case of amœbic liver abscess, possibly contracted in Siam, successfully treated with chloroquine. So far there have been reported thirty-two cases of intestinal amœbiasis, twenty-one of hepatitis, and two cases of liver abscess treated with this new drug.

Since hepatic amœbiasis is of frequent occurrence in Siam, usually admitted to hospitals in the abscess state, the author has had the opportunity to try the use of chloroquine in nine patients in the Siriraj Hospital, all with liver abscesses. Results have been very promising, as may be seen from the following summaries:

Plan of treatment.†—Conan (1949) recommended an oral regimen with a priming or loading dose of 0.6 gm. of chloroquine base daily for two days, followed by 0.3 gm. daily for twelve or nineteen days, the complete course lasting fourteen or twenty-one days. The treatment employed by the author followed these suggestions, but in severe cases the initial dose was prolonged until conditions improved before changing to the lower dose.

* From the Department of Internal Medicine, Faculty of Medicine, and Siriraj Hospital, University of Medical Sciences, Bangkok, Siam.

Presented at a General Meeting of the Siriraj Hospital on the 27th August, 1949.

† Chloroquine used here was the diphosphate, under the name of Aralen (Winthrop Products Inc.), supplied by the American Presbyterian Mission, each tablet of 0.25 gm. containing 0.15 gm. of chloroquine base.

In all cases good response was obtained. Within a few days after beginning the treatment the general condition of the patients improved; fever and pain subsided; the liver retracted under the costal margin; and the leucocytosis receded. All patients gained considerably in body weight before their discharge from hospital. Two of them, however, developed complications, and it is thought worth while to present a brief summary of their case histories.

Case reports

Case 1.—A Chinese male, 48 years old, settled in Siam for about 25 years, admitted on the 28th March, 1949, for pain and tenderness in the right lower part of the chest. Past history disclosed amœbic liver abscess two years previously, treated with emetine and liver puncture in our hospital. The present illness was of one month's duration. Physical examination revealed an enlarged and tender liver, a moderate fever (38 to 39°C.), with pulse rate of 80 and respiration of 30, arterial blood pressure 104/62, total leucocyte count 12,500, with neutrophils 82 per cent and lymphocytes 18 per cent. Blood film, urine and faeces yielded negative findings. Fluoroscopy found the diaphragm limited in excursion, with the right dome elevated to the level of the 8th rib posteriorly. The provisional diagnosis was amœbic liver abscess of the right lobe. Liver puncture brought out 320 cc. of creamy, chocolate-coloured pus. Emetine hydrochloride was begun in daily doses of half a grain, but had to be interrupted after seven days because of prostration and hypotension (86/52 mm. Hg.). After an interval of one week the injection was resumed, but again had to be stopped after seven doses. The liver was still tender and protruded two finger-breadths below the costal margin. The afternoon temperature was around 39°C., and the leucocyte count was between 10,100 and 12,250, with neutrophils 80 per cent and lymphocytes 20 per cent. Roentgenography revealed the abscess bursting into the sub-diaphragmatic area. Since the patient was sensitive to emetine, and secondary infection was suspected, energetic treatment with liver puncture, penicillin, sulfathiazole and subsequently streptomycin was instituted, but to no avail. Fever and leucocytosis remained unchanged.

At this stage it was decided to try chloroquine. The course followed was 0.6 gm. of the base daily for three days, followed by 0.3 gm. daily for twelve days, giving a total dose of 5.4 gm. Four days after beginning the treatment the temperature returned to normal and the patient showed marked improvement in general (see chart 1). Pain and tenderness over the liver subsided, and the patient rapidly put on weight. He was discharged on the 11th July, 1949. Examination before discharge revealed

that the liver had retracted under the costal margin; by roentgenography, the right dome of the diaphragm was found slightly elevated still.

10 ee. of sterile, thick pus, resembling anchovy sauce. To reveal the extent of the abscess cavity iodized oil was injected, 2 ee. each of the

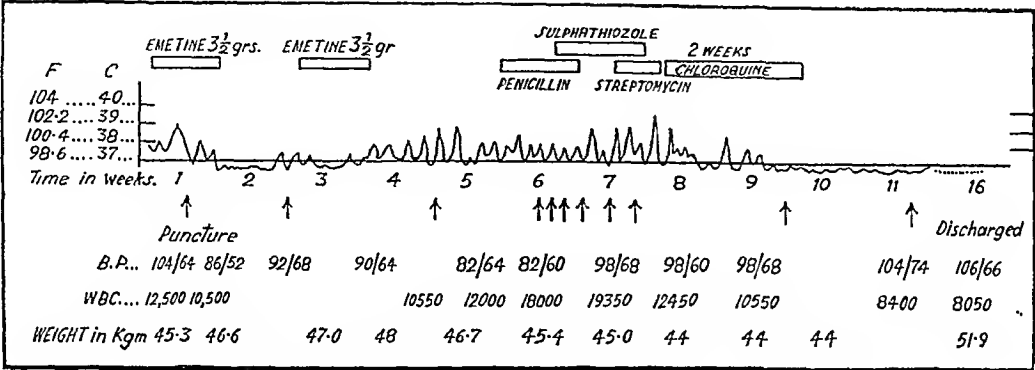


Chart 1.—Case 1, first admission, 28th March to 11th July, 1949.

After staying at home for fifteen days, however, the patient developed a violent cough and expectorated blood-stained, purulent sputum. He came back on the 6th August, with a temperature of 38.8°C., and a leucocyte count of 10,700. The liver was not palpable. X-rays disclosed elevation of the right dome of the diaphragm with localized consolidation in the base of the right lower lobe of the lung (see figures 1 and 2, plate VIII). The sputum

10 per cent and of the 40 per cent preparation. Subsequent roentgenogram showed a lung abscess in connection with the liver abscess (see figure 2, plate VIII). After five days of medication the patient began to improve rapidly. Coughing stopped, and fever and leucocytosis subsided. He was fairly well on 27th August, when x-rays revealed a small remnant of the opaque medium in the liver and in the lung (figure 3, plate IX).

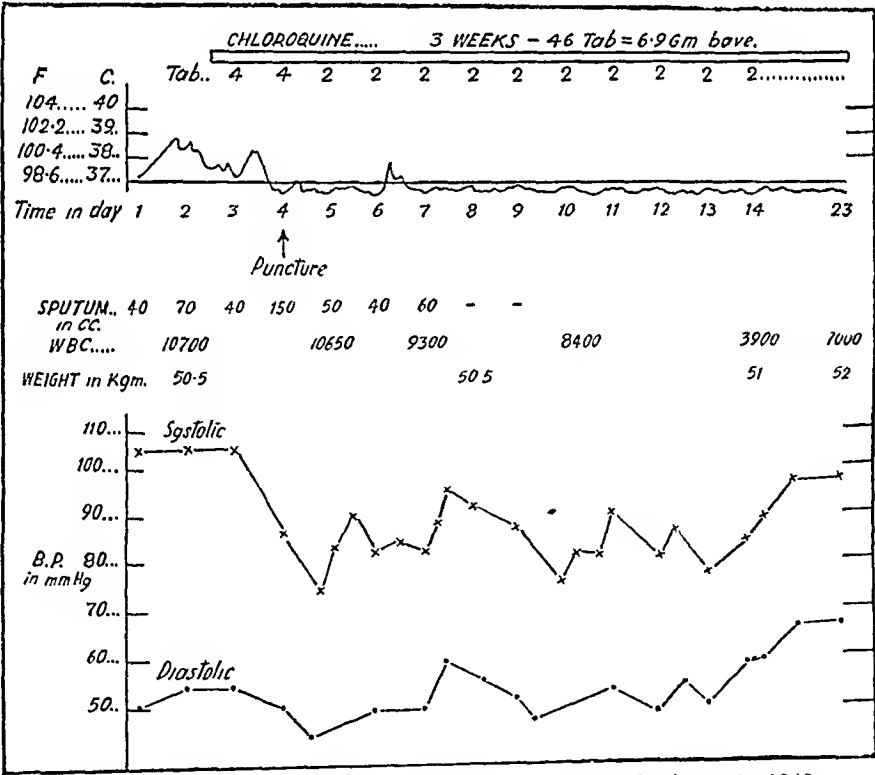


Chart 2.—Case 1, second admission, 6th to 27th August, 1949.

was anchovy sauce in character, amounting to 40 to 70 ee. daily. The diagnosis was recurrent amoebic liver abscess with secondary pulmonary amoebiasis. Chloroquine was administered in doses of 0.6 gm. of the base daily for two days, then reduced to 0.3 gm. daily for nineteen days. On the second day of treatment the fever stopped. Liver puncture yielded with difficulty

Case 4.—A Siamese male, 48 years old, entered the hospital on 8th July, 1949, with the complaint of a painful and tender mass over the upper part of the abdomen for about two months. He admitted passing bloody and mucous stools about three years before admission. Two months prior to the admission he had slight fever with some pain over the epigastrium,

followed two days later by the appearance of a hard and tender mass with increase in the fever. Physical examination revealed a slightly tender fluctuating mass, size about 4×5 inches and protruding about 3 inches in the epigastric region (see figure 4, plate IX). The liver was palpable, extending about two finger-breadths below the right costal margin. The base of the right chest had relative dullness and diminished breath sounds. The body temperature was 38.5°C ., pulse rate 105 per minute, respiration rate 22 per minute and the arterial blood pressure was 96/72. The white blood count was 11,500, neutrophils 78 per cent and lymphocytes 22 per cent. There were hook-worm ova in the faeces, but no *Entamoeba histolytica*. Intravenous hippuric acid synthesis liver function test gave 0.33 gm. in the first hour. Fluoroscopy revealed a large mass in the epigastrium and marked elevation and fixation of the right dome of the diaphragm. The provisional diagnosis was amoebic liver abscess of the left lobe.

Liver puncture on the mass yielded 400 cc. of thick, creamy, chocolate-coloured pus, free from *Entamoeba histolytica* and bacteria. On the sixth day of hospitalization, chloroquine was administered, 0.6 gm. of the base daily. The following day the patient developed severe coughing and expectorated about 300 cc. of chocolate-coloured sputum. He also had dyspnoea and weakness with rapid, feeble pulse. The temperature rose to 39.5°C . (see chart 3). Heart stimulants were administered. It was suspected that there might be another abscess in the right lobe of the liver, which had burst into the right lung. Liver puncture was performed into the right lobe and 300 cc. of

characteristic pus were obtained. X-rays showed two abscess cavities, right and left, with partial pulmonary consolidation over the lower lobe of the right lung (see figure 5, plate IX).

Because of these developments, the dose of 0.6 gm. of chloroquine daily was continued. Five days later it was observed that the arterial blood pressure was becoming progressively low, viz, 104/74, 96/72, 94/62, 84/52 and 78/52. Although the patient made no complaint, this was considered to be a toxic manifestation of the drug. On the sixth day the blood pressure came down to 72/52 and on that account the medication was interrupted. The total amount of drug given was 3.315 gm. of chloroquine base. The white blood count was 8,100, neutrophils 76 per cent and lymphocytes 24 per cent; the chocolate-coloured expectoration had nearly stopped, and the temperature had returned to normal. After two days' interval the blood pressure returned to 92/64. The drug was then continued, 0.3 gm. of the base being given daily for fourteen days longer. The patient improved rapidly. After eighteen more days in the hospital, having gained 2.0 kg. in weight and the liver function test yielding normal result (0.91 gm. of hippuric acid in the first hour), he was discharged in a quite healthy condition, although roentgenogram still showed a slight elevation (figures 6 a, b, c, plate X) of the diaphragm, with complete clearing of pulmonary consolidation in the lung.

Of the remaining seven cases all had amoebic abscess in the right lobe of the liver. They were treated with chloroquine according to the schedule of Conan and all improved rapidly without incidents.

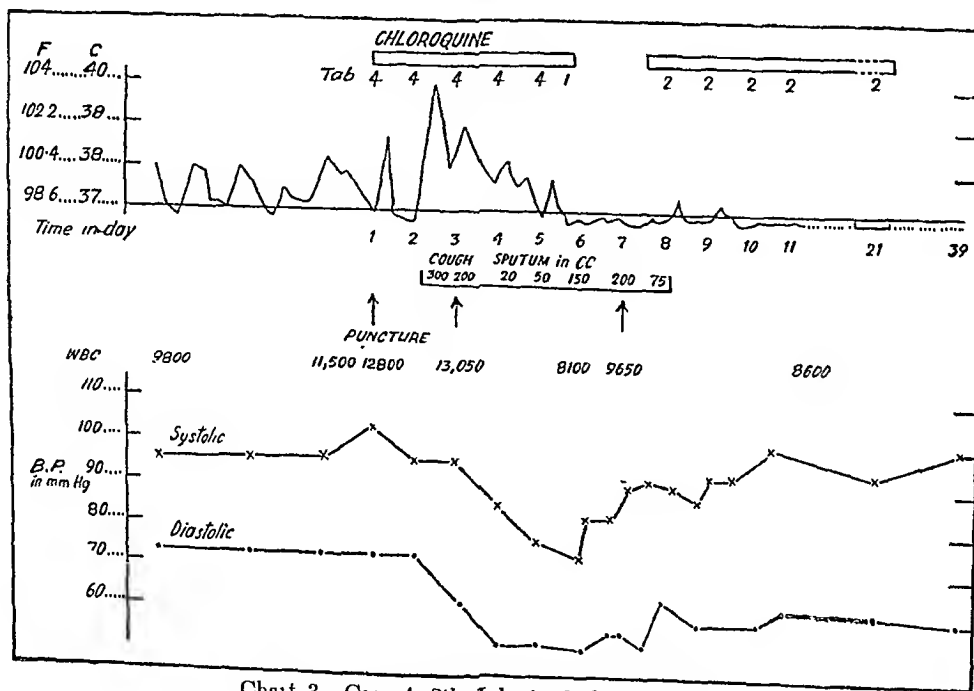


Chart 3.—Case 4, 8th July to 28th August, 1949.

Toxicity of chloroquine.—Conan (1949) observed minor toxic manifestations in five of his forty patients. Three had nausea, one transient pruritus and one disturbance of ocular accommodation. In antimalarial doses (1.2 to 1.5 gm. of the base for one to three days) symptoms of toxicity of the drug are also occasionally observed but are usually mild and transient. In the present series, none of the above-mentioned symptoms was found. But while treating case 3 it was observed that the arterial blood pressure was gradually declining. By the third day of the treatment the systolic pressure had dropped from 98 to 80. The patient, however, made no complaint, and the medication was continued. After the course was finished the blood pressure returned to normal. In case 4 there was a more marked drop of the blood pressure as mentioned before, so that treatment had to be interrupted. The medication could be resumed, however, until completion of the course, without further fall in the blood pressure. In five other cases also the blood pressure dropped during the first week of the medication, the greatest fall in each case being as follows: Case 5, 14 mm., case 6, 10 mm., case 7, 18 mm., case 8, 18 mm. and case 9, 12 mm.

Record of the pulse rate and pulse pressure during the periods of hypotension showed that they were not remarkably altered. Evidently the lowering of the blood pressure was not directly connected with the heart rate. In all cases before the medication there was slightly rapid pulse due to toxic effects of the disease; but a few days after beginning the drug the patients usually improved and the pulse rate returned to normal, although the blood pressure was low.

Comments

It is to be observed that from none of the liver abscesses could the *Entamoeba histolytica* be identified, but the diagnosis in all cases was substantiated by the characters of the pus obtained by puncture. In four cases characteristic creamy, chocolate-coloured pus was obtained; in the remaining five cases the pus was slightly greenish-yellow. All pus samples were sterile. Iodized oil was introduced into the abscess in five cases to enable visualization of the cavity by means of x-rays (figure 7, plate XI).

All nine patients were male. All except one (case 3) admitted a past history of dysentery, but during the admission only one patient (case 6) had *Entamoeba histolytica* in the stool.

Results obtained with chloroquine are highly promising. The patients showed improvement after a few days of treatment. Pain and tenderness over the liver soon disappeared. The temperature and the leucocyte count returned to normal. The appetite improved and the patients gained in weight before discharge.

It is remarkable that while the usual toxic symptoms as observed by other workers were absent in the present group of patients, a hitherto undescribed effect, *viz.*, lowering of the arterial blood pressure, was observed in eight cases. Although this was not accompanied by any subjective symptom, it was necessary to stop the drug temporarily in one patient. No detectable alteration in the work of the heart was observed, and Ketushin of the Department of Physiology, studying the action of chloroquine

TABLE

Summary of clinical and laboratory data, and results of treatment of amœbic liver abscess with chloroquine

Case number	Age	Duration of illness before admission in days	Afternoon temperature, °C.	Liver palpable in finger-breadths	W.B.C.	Neutrophil	Liver function test. Intra-venous hippuric acid synthesis in first hour	Febrile in days after beginning the drug	Course of treatment in weeks	Weight gained during treatment in kg.	
1	48	60	39.5	2	16,400	87	..	4½	2	7.9	1st admission.
			38.8	Negative	10,700	68	0.25	1½	3	1.5	2nd admission.
2	50	90	39.0	4	12,100	72	..	2	2	6.5	
3	42	90	39.0	2	11,050	90	..	2	2	7.0	
4	48	60	38.2	2	12,800	80	0.33	5	3	2.8	
5	48	20	38.5	3	20,450	83	0.42	9	3	3.0	
6	40	30	38.0	4	7,400	87	0.26	3	3	1.0	
7	40	13	37.2	Palpable	10,800	84	0.39	0	2	2.8	
8*	60	13	37.3	1	7,700	74	0.28	0	2	0.5	
9	38	60	37.8	2	17,500	91	0.37	4	2	1.0	

*Discharged after 7 days of medication. One more week of treatment was continued at home. Three weeks after the termination of the course he came for re-examination and was found to be very well.

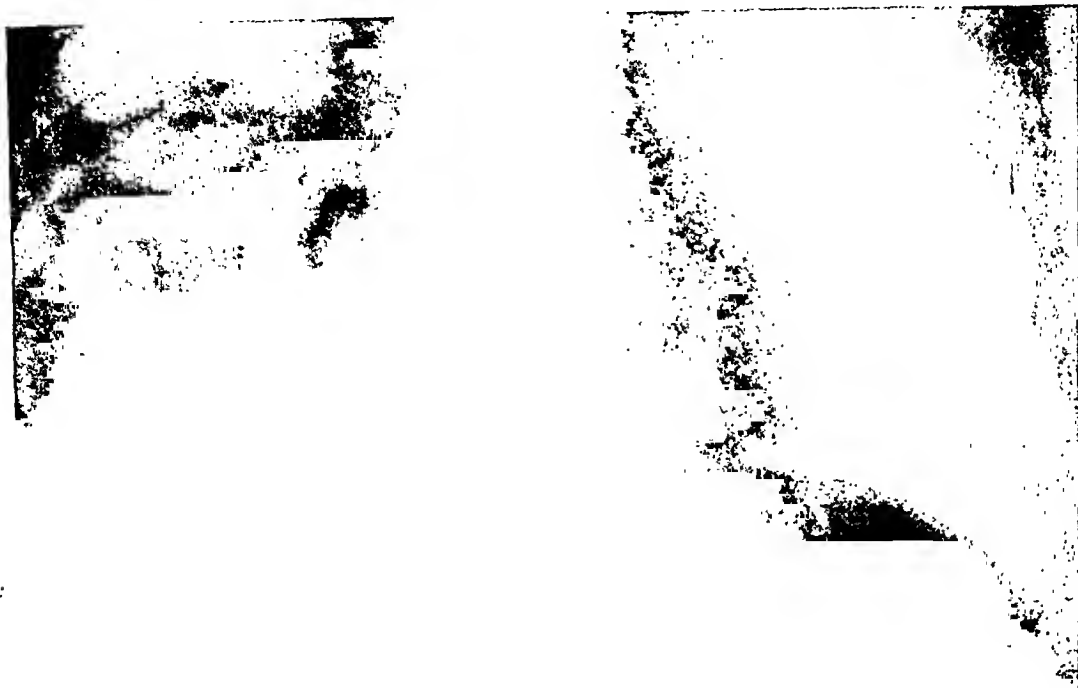


Fig. 1.—Case 1, before treatment (6th August, 1949), showing localized consolidation in the base of the right lower lobe of the lung.

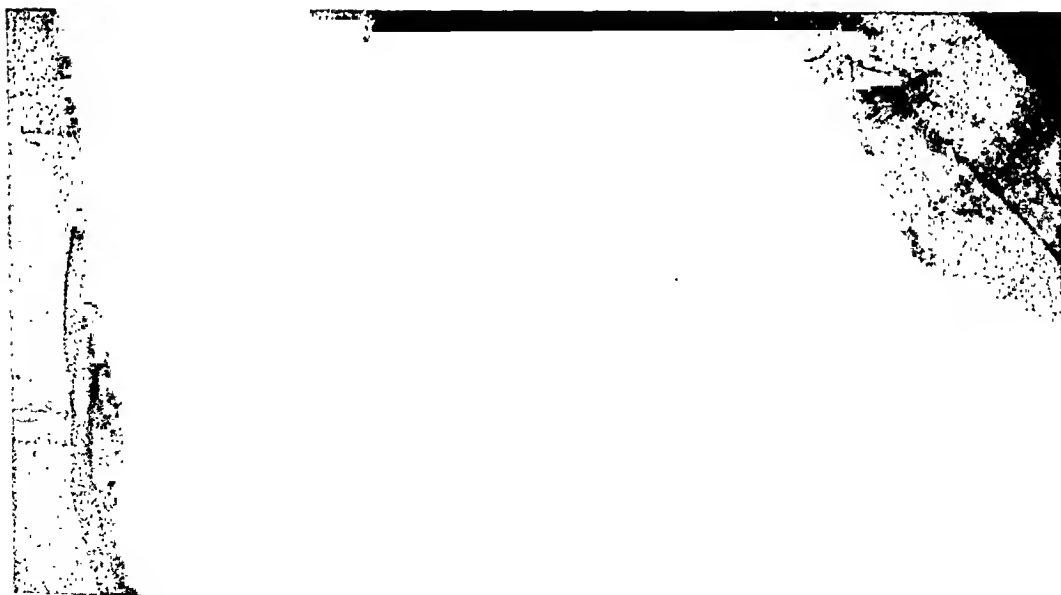


Fig. 2.—Case 1, during treatment, showing liver and lung abscess cavity visualized by x-ray after introduced air 40 per cent and 10 per cent iodized oil.

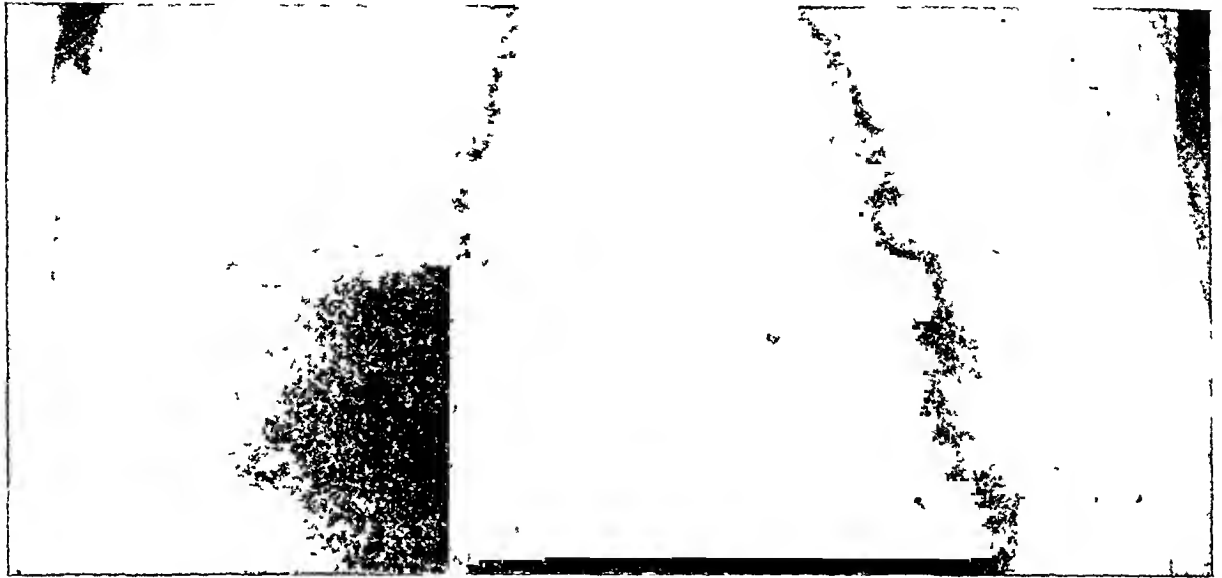


Fig. 3.—Case 1, after treatment, 27th August, 1949.



Fig. 4.

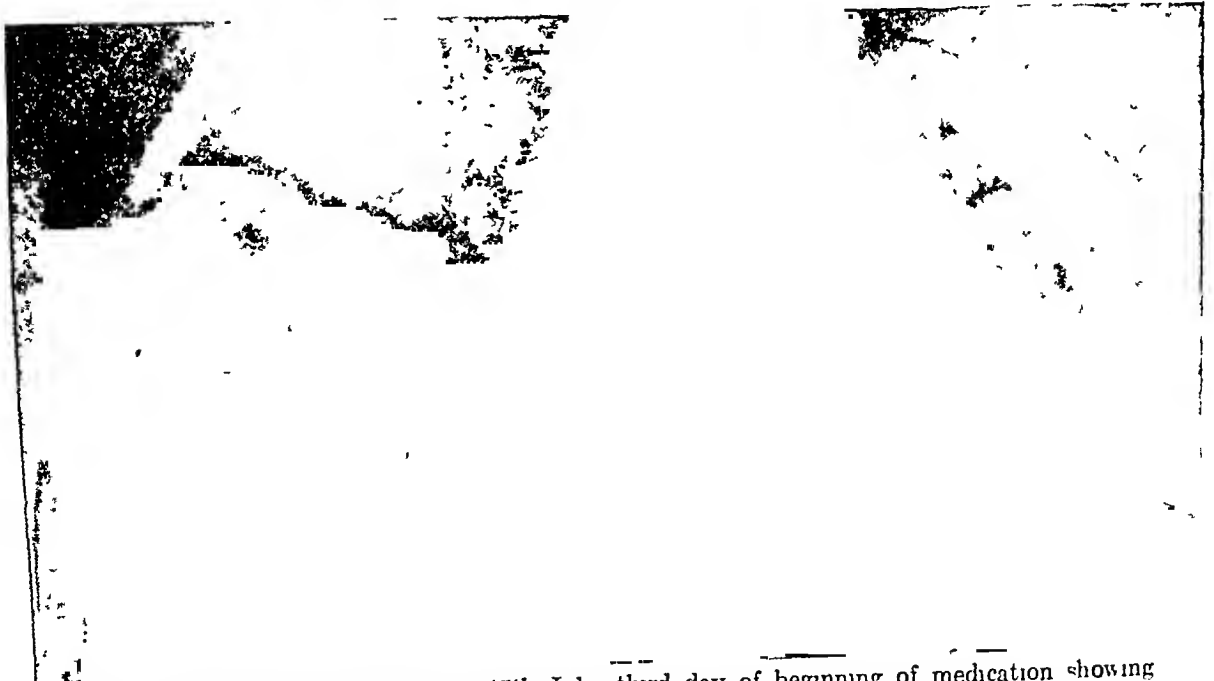


Fig. 5.—Case 4, during treatment, 15th July, third day of beginning of medication showing two abscess cavities in right and left lobes of the liver with partial pulmonary consolidation over the right lower lobe of the lung

PLATE X
CHLOROQUINE IN THE TREATMENT OF AMOEBIC LIVER ABSCESS : C. HARINASUTA.
(O. A.) PAGE 37



Fig. 6a.—Case 4, after treatment.



Fig. 6b.—Case 4, after treatment.



Fig. 6c.—Case 4, after treatment.

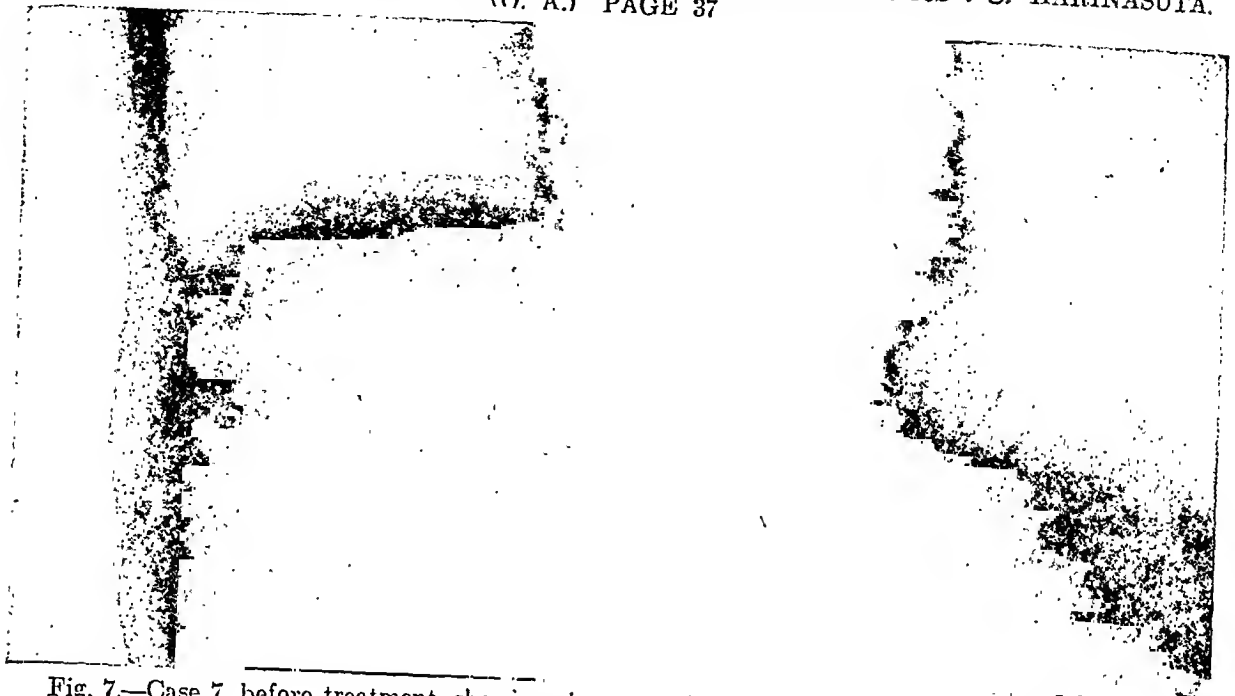


Fig. 7.—Case 7, before treatment, showing abscess cavity visualized by x-ray after introduced air and iodized oil.

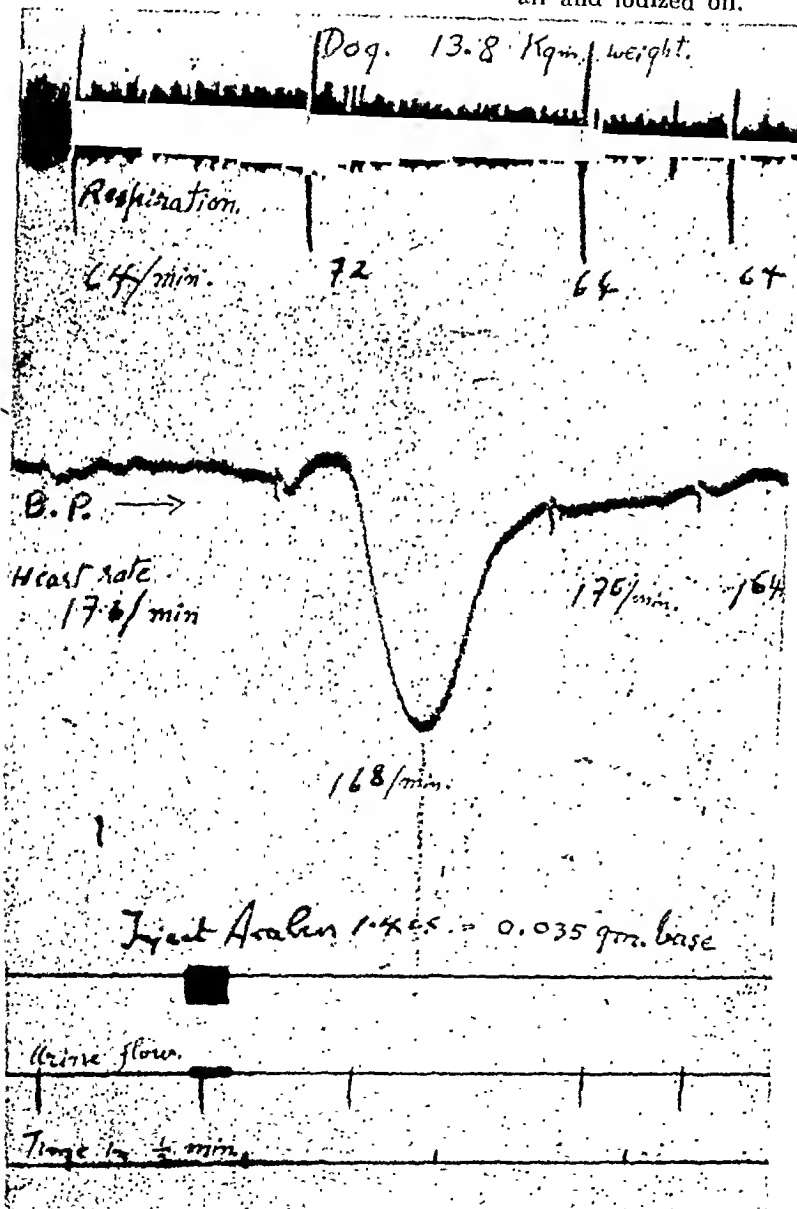


Fig. 8.—Showing action of chloroquine (Aralen) on the circulation of a dog. Before drug blood pressure = 114 mm. Hg. After drug blood pressure dropped to 56 mm. Hg.

on the circulation of a dog (see figure 8, plate XI), found that intravenous injection of the drug caused a marked drop in the blood pressure without significant change in the heart's action. Possibly the effect was brought about by vasodilatation.

Summary

1. The report covers nine cases of amoebic liver abscess, two with pulmonary complications, treated with chloroquine with promising results.

2. The dosage regimen of Conan was followed in essentials.

3. In all cases a good response to the drug was observed within a few days of the medication, as seen from improvement in general condition, return to normal of the temperature and the leucocyte count, subsidence of local symptoms and subsequent gain in body weight.

4. A hitherto unobserved manifestation was noted during the use of chloroquine, viz, progressive fall in the blood pressure. In one case this reached a dangerous level, necessitating interruption of medication. It was possibly due to a toxic action of the drug, causing dilatation of the blood vessels.

I wish to express my gratitude to my chief, Dr. P. Kangsadin, for permission to carry out this study; to Dr. O. Ketusinh, Head of the Department of Physiology, for facilities in laboratory work; to the Dean of the Faculty of Medicine and Siriraj Hospital, for endorsement of publication; to the American Presbyterian Mission for supplying the drug, and to the House Officers who assisted in the work.

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INTENSIFIED ELECTRICAL CONVULSIVE THERAPY IN A MILITARY HOSPITAL

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THORPE (1947) of West Riding Mental Hospital, Wadsley, Sheffield, in January 1947, advocated the use of multiple E.C.T. shocks in acute mania. Three to 6 shocks daily were given with favourable results. Tyler and Lowenbach (1947) of Duke University Hospital, Durham, published their results of polydiurnal electric shock treatment in mental disease in September 1947. As many as 4 treatments were given daily for several days in succession sufficient to produce mental confusion and

maintain it for at least a week. In their opinion the treatment proved no more dangerous than other forms of shock therapy. Results in 32 patients compared favourably with results obtained by classical method of giving E.C.T. twice or thrice weekly and the number of hospital days was considerably reduced.

Heuyer, Lebovici and Amado (1948) also reported favourable results with this method and gave as many as 6 shocks in a day to some of their patients. They specially mentioned the case of a girl suffering from recurrent manic attacks for 6 months. Each attack remitted with a series of 5 to 6 shocks given in the usual manner, i.e. once every 2 or 3 days. The patient had had 5 relapses when the summation method was tried with 4 shocks daily for 3 days. After a period of confusion the patient became normal and was followed up for 6 months when the recovery was maintained.

Page and Russell (1948) investigated the effect of increased voltage and duration on more than 300 patients. They worked on a fixed standard of 150 volts and the time of 1 second. One + several shocks, i.e. one convulsion, and a number of additional stimuli in the primary convulsion in quick succession were given and treatment repeated daily. This treatment was stopped as soon as there was a remission or a profound confusion, i.e. when the patients' habits became faulty. The average number of treatments per patient was observed to have been halved by the new technique and so was the average number of days under treatment by each patient. The authors also claimed that risk of fractures was less with the new treatment. In some cases (acute mania) the procedure had to be repeated once or twice the same day.

Kennedy and Anchel (1948) reported favourable results in 25 chronic schizophrenics who had shown no response to previous courses of insulin or E.C.T. or a combination of the two. They aimed at a regression, which was considered deep enough when the patient wetted and soiled or acted like a child of four. Treatment was stopped at this stage and confusion began to clear.

Inspired by the published work of these pioneer workers and also because, owing to the posting away of my assistants and the trained nursing sisters insulin treatment had to be discontinued, I started giving intensified E.C.T. to my patients at the Military Hospital, Poona, in July 1948, following the method advocated by Page and Russell (1948), i.e. by giving 1 + several shocks (with 150 volts \times 1 second) with an Ediswan machine, commencing with 1 + 5 shocks daily and increasing it to as many as 1 + 13 shocks. The treatments were given daily. Fifty-eight patients have been treated with this method so far. Thirty-nine were cases of schizophrenia of various types, 9 of manic-depressive psychosis, and 10 of psycho-neurosis, mostly reactive depressions and

hysteria. Seven including 3 cases of paranoid type of schizophrenia, *i.e.* 12 per cent, showed no improvement at all. Twelve cases, *i.e.* 20.7 per cent, showed only a slight improvement. Twenty-two, *i.e.* 38 per cent, made complete social recoveries. (This included 12 cases of schizophrenia.) Seventeen, *i.e.* 29.3 per cent, showed a definite and marked improvement. The average number of treatments per patient was 13.3 and the maximum in this series was 48. The actual number of days of stay in hospital in these cases would be fallacious as it depended on several extraneous factors like the holding of the medical board, the approval of the papers by the A.D.M.S. and the disposal by the units and depots, etc. But if calculated from the first day of treatment to the date of the medical board in the case of psychotics who under the existing regulations have to be invalided and to the date of return to duty in other cases, the average number of days in hospital per patient comes to 40.8.

The results have been compared with those obtained in 55 cases treated during the period November 1947 to June 1948, by the old method, the following table :—

Intensified E.C.T. results

Type of cases	Method	Number of cases	Average number of treatments	Average number of days in hospital	Percentage showing complete social recovery	Percentage showing marked improvement
Schizophrenia (various types)	Old	32	18.8	81.4	9.3	31.2
	New	39	16.2	51.5	33.3	23.0
Manic-depressive psychosis ..	Old	10	16.2	68.4	20.0	80.0
	New	9	11.8	28.3	44.4	55.6
Psychoneurosis (hysteria and reactive depression).	Old	13	5.5	35.0	61.5	38.5
	New	10	3.3	10.7	60.0	20.0

These results show that the average number of days under treatment by each patient is considerably reduced with the intensified method. The percentage of cases of schizophrenia and manic-depressive psychosis, showing complete social recovery, has also increased significantly.

Valentine (1949) also considers that in certain cases treatment twice or three a week is too infrequent for the cumulative phase to occur and that intensive E.C.T. helps to shorten the period of hospitalization in such cases.

Two cases are of special interest :—

Case 1.—An 18-year-old son of a medical officer, who had three previous breakdowns of schizophrenic reaction type and who was also suffering from allergic asthma and had failed to respond to 3 courses of classical E.C.T., responded speedily to this method and was discharged from hospital within two weeks of the start of the intensified treatment. This was one of the earliest cases of the series and I was somewhat reluctant to try this method on him

especially in view of his asthma, but the result was very encouraging indeed. I have followed up this patient for over a year now. His mental condition has been normal since his discharge though his asthma is as bad as ever.

Case 2 was that of a recruit aged 17 years, with less than two weeks' service and having an unstable family history, who broke down while under military training with a typical schizophrenic reaction, and was admitted for treatment in May 1948. Two courses of E.C.T. by the time-honoured method did not result in any improvement. Intensified E.C.T. resulted in a complete regression to infancy when it was discontinued and patient completely came round in 2 weeks. His mental condition became quite normal; but he developed a lung abscess during the course, probably due to inhalation of some particles of food during a convulsion. This was successfully treated with two courses of penicillin and sulphamezathine and he was discharged 9 months after admission.

My experience with the intensified E.C.T. is no doubt limited but the results have been encouraging and indicate that further trials are

worth while. No untoward accidents were met with.

Summary

1. Intensified electrical convulsive treatment was tried in 58 cases with encouraging results.
2. A brief description of two of the cases is given.

My thanks are due to Colonel E. A. R. Ardesir, O.C., Military Hospital, Poona, for his interest in the above work, the Nursing Staff for their assistance and co-operation, and to the D.M.S. Army for permission to publish this paper.

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Note.—The Ediswan machine is commonly used in mental hospitals in India. It has various gadgets controlling the voltage from 70 to 150 volts and time from 0.1 to 1 second. It can be had from Messrs. Cox-Cavendish Electrical Co., Ltd., 45-47, Marylebone High Street, London, W.1. Other similar machines are equally useful for intensified E.C.T. by the method described above, provided the voltage and time range up to 150 volts and 1 second respectively.

STUDIES ON SEX HORMONES

Part I

SPERM TEST OF PREGNANCY UTILIZING MALE TOAD, *BUFO MELANOSTICTUS SCHNEID.*, AS TEST ANIMAL

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and

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In the early months of pregnancy there is no single sign nor any combination of signs and symptoms to make the diagnosis unequivocal. To overcome this difficulty, a number of tests, biological, biochemical and immunological, have been tried. Of these only three biological tests, viz, Aschheim-Zondek, Friedman and Hogben, have come to stay. The consensus of opinion is that all other tests such as bitterling test (Naidu and D'Souza, 1944), the various intra-dermal tests (Editorial, 1937; Gilli and Howkins, 1937), pregnanediol test (Day and Cains, 1948; McCormack, 1946; Morrow and Benua, 1946), etc., are fallacious and unreliable. The three standard biological tests, viz, A-Z, Friedman and Hogben, suffer from the disadvantages that they are expensive, time consuming, complicated and can only be performed in well-equipped laboratories under skilled hands. Moreover, in case of Hogben test the unavailability of the test animal, *Xenopus laevis* Daud., outside South Africa, is a serious drawback. The consideration of time factor, above all, is all important, particularly so in the management of emergent cases where these biological tests are of little use as their results can only be known at the earliest after 4 days, 2 days and 1 to 2 days respectively (Crew, 1939; Landgrebe and Hobson, 1949; Weisman *et al.*, 1942).

Two modifications of A-Z test have been reported (Hoffman, 1946; Soman, 1944, 1946; Zondek *et al.*, 1945). In these tests, white immature rats are used and the end-point is ovarian hyperaemia instead of appearance of mature follicles or corpus luteum. But the reliability of the tests still awaits confirmation. Even if these tests prove reliable, they are not free from other disadvantages of the standard biological tests.

Recently, Galli Mainini (1947) reported a new biological test of pregnancy. It is based on the reaction of a species of male toad, *Bufo arenarum* Hensel., in shape of ejaculation of sperms when untreated pregnancy urine is injected into it. Other South American workers (Alejandro, 1947; Pinto and Suer Boero, 1948) have corroborated his findings. The test, as reported, seemed to be very accurate, extremely simple, inexpensive, very rapid and highly specific. At that time it seemed to us that the greatest drawback of the test, like that of the Hogben, may be the non-availability of the toad in countries outside South America. In order to find out if any of the locally available species of toads and frogs can be successfully used to replace *B. arenarum* in carrying out this test, it was thought worth while to make a systematic study. This report is based on such trial and embodies the results of our investigations with *Bufo melanostictus* Schneid., the common toad of Orissa (also widely prevalent throughout India, most parts of Pakistan, Ceylon, Burma, Malay, Thailand, Indo-China, South China and Indonesia) and was carried on during the period of 8 months from February to September 1949.

Method

Untreated samples of urine were subjected to qualitative physical and chemical tests. Healthy male toads, weighing 50 to 70 gm., were put each into a cylindrical glass jar (12 inches high by 8 inches diameter), covered with wire gauze held secure by weight and duly marked with the respective number. By means of a bent glass catheter, samples of urine from the cloaca of each toad were withdrawn and examined under microscope for presence of sperms before the injection of urine. This procedure ensured against any fallacy as each animal served as a control of its own.

By trial and error in the beginning it was found out that it is better to utilize three toads for each specimen of urine in order to guard against occasional refractory and non-reactive animals as well as death of one after injection.

Each toad was taken in turn and 10 mil. of untreated urine from the corresponding sample was injected into its dorsal lymph sac by means of a hypodermic syringe and a small haemostat applied for half a minute or so over the point of needle puncture to prevent leakage. After $\frac{1}{2}$ hour, by catheterization, cloacal samples from each toad were taken and examined microscopically for the presence of sperms. A sample was considered positive if any one or more of the three toads used showed sperms in the cloacal samples. If negative, fresh cloacal samples were examined every half hour till 4 hours. If still negative, the urine was treated otherwise for extraction of hormone according to the method of Barbosa de-Castro (1947) with the modification that rectified spirit was used in place of absolute alcohol (hereinafter

referred to as 'hormone extraction method' or 'extraction method'); 100 mil. of urine from each specimen were subjected to this treatment and the extract injected into two additional toads. Specimens of urine treated and untreated from puerperal cases were injected into toads using the same technique.

Urines from healthy regularly menstruating women in various phases of menstrual cycle, from healthy males and samples of frog saline* were also similarly subjected to the test in order to find out if any of these gave positive reaction.

Samples of urine of known and suspected cases of pregnancy and of puerperal cases were obtained from the obstetrics wards and ante-natal clinics of the college hospital and from private sources. Non-pregnant urines were collected from the nursing staff while male urines were secured from members of the staff and others.

Lastly, in order to find out the particular hormone or hormones responsible for this biological reaction and the degree and nature of its specificity, trial was made with standardized preparations of various hormones in varying doses, viz, chorionic gonadotropin of pregnancy urine, œstrone, œstriol, progesterone, stilbœsterol and desoxycorticosterone.

Further, with a view to knowing whether the used toads can be re-utilized after rest and with proper feeding for a few days under artificial conditions, the following method was tried :

Housing and feeding the toads.—Toads already subjected to test were placed in a galvanized iron tank containing 4 inches to 6 inches deep water and provided with taps for emptying and refilling water daily. The cover of the tank was fitted with wire netting of 1 inch mesh. Inside the tank there were two ladders leading to two platforms fixed to its sides. A narrow piece of wood bridged the two platforms. An electric bulb was provided inside the tank. The windows of the room containing the tank were kept open at night and the electric light of the tank was kept burning when other lights were put out. The whole idea was to attract insects to the tank so that the toads could help themselves to them. This device has proved a success. The toads are getting on fairly well for the last two months and are being utilized every 10 to 12 days with satisfactory results.

In the beginning mortality of the toads was 9.26 per cent with untreated urine. With the idea that the bacterial content of urine might be one of the causes of mortality, we started adding 5 drops of 20 per cent thymol in alcohol to each 100 mil. of urine. The toads tolerated the thymol satisfactorily without any change in their reactivity. Reaction of the toads as

regards ejaculation of sperms to injections of thymol solutions in frog saline or thymol solution added to male and non-pregnant urine was studied and was always found to be negative.

Observations

Positive cases were characterized by the presence of sperms in cloacal samplings when examined microscopically. The sperms are elongated curved bodies with a flagellum or tail springing from the middle piece and their movement is quite brisk and characteristic of the positive cases. 87.98 per cent showed presence of sperms in $\frac{1}{2}$ to $1\frac{1}{2}$ hours after injection, the earliest being 25 minutes and the latest 4 hours.

In all, 407 specimens of urine were subjected to this test. Of this, 63 samples from 43 suspected cases of early pregnancy and 262 specimens from 108 known cases of pregnancy were examined. In addition, 26 specimens collected from 6 cases on different days of early puerperium and 36 specimens collected during various phases of menstrual cycle from 12 healthy regularly menstruating women and 20 samples of male urine were also tested.

Suspected early cases.—Of the 63 samples from 43 suspected cases of early pregnancy, subsequent history proved 4 to be cases of delayed menstruation, 3 others turned out to be cases of amenorrhœa due to causes other than pregnancy and 1 was a case of incomplete abortion. Sixteen samples from these 7 cases, both by treated and untreated methods, gave persistently negative results and one sample from the case of abortion gave negative result with untreated urine. Of the remaining 46 specimens of urine from 35 cases of early pregnancy, confirmed by subsequent history, 44 (from 33 cases) showed positive results with untreated urine and two samples collected 5 days and 8 days after missed period from 2 cases gave positive reaction by hormone extraction method (*vide table I*); these two cases might be too early with very little chorionic tissue to give satisfactory concentration of hormone in urine to be positive by untreated method.

The case of abortion referred to above is an interesting one. The patient was admitted to the hospital on 16th August, 1949, with complaint of intermittent bleeding accompanied by pain of 10 days' duration preceded by history of 3 to 4 months' amenorrhœa. Examination of urine of this case by hormone extraction method could not be done as the quantity was small and before collection of further sample, the abortion became complete. The products of conception along with the decidua came out *en bloc* as a cast of the uterine cavity. Detailed study of this cast is being carried on by workers of other departments of this college. Private discussion with these workers has revealed that the fœtus seems to be of much earlier age than the period of amenorrhœa.

*0.6 per cent sodium chloride solution in distilled water without any adjustment of pH.

Clinically undoubted cases of pregnancy.—The clinical diagnosis of the 'known' cases was unequivocal. All of them were in-patients of the hospital and their period of gestation varied

The consideration of tables I and II reveals that, in a series of 308 samples from 143 cases of early and late pregnancy, the result was cent per cent positive.

TABLE I

Showing results obtained with urines of early cases of pregnancy confirmed by subsequent history

Period of gestation (after missed period)	Num- ber of cases	Results with						Net result (total)	
		Untreated urine			Treated urine*				
		Number of samples tested	Number of samples positive	Per- centage of samples positive	Number of samples tested	Number of samples positive	Per- centage of samples positive	Number of samples positive	Per- centage of samples positive
5 days ..	1	1	nil	..	1	1	100.0	1	100.0
8 " ..	1	1	nil	..	1	1	100.0	1	100.0
8 " to 2 weeks ..	4	5	5	100.00	5	100.0
3 to 8 weeks ..	17	25	25	100.00	25	100.0
9 to 14 " ..	12	14	14	100.00	14	100.0
TOTAL ..	35	46	44	95.65	2	2	100.0	46	100.0

* 'Treated urine' means urine subjected to hormone extraction method, and only specimens giving negative results with untreated urine were subjected to this treatment.

from 20th to 40th week. Of the 262 samples collected from this group, 234 gave positive results with untreated urine; the remaining 28 became positive by hormone extraction method. These 28 specimens were collected a few hours to 5 weeks before the onset of labour from 12 cases (see table II).

Puerperal cases.—Examination of samples of urine collected during early puerperium, as presented in table III, shows that most of them became negative after 4th day; only one sample gave positive result up to the 8th day of puerperium by treated method. In this exceptional case, some live chorionic tissue

TABLE II

Showing results obtained with urines from undoubted cases of pregnancy in later half of the term

Period of gestation in weeks *	Number of cases	Results with						Net result (total)	
		Untreated urine			Treated urine				
		Number of samples tested	Number of samples positive	Percentage of samples positive	Number of samples tested	Number of samples positive	Percentage of samples positive	Number of samples positive	Percentage of samples positive
20-28	11	30	30	100.00	30	100.0
29-36	32	110	108	98.18	2	2	100.0	110	100.0
37	13	32	30	93.75	2	2	100.0	32	100.0
38	15	29	25	86.21	4	4	100.0	29	100.0
39	18	33	24	72.73	9	9	100.0	33	100.0
40	19	28	17	60.71	11	11	100.0	28	100.0
TOTAL	108	262	234	89.31	28	28	100.0	262	100.0

* Calculated from the first delivery of the pregnancy.

* Calculated from the first day of the last menstruation.

TABLE III

Showing results obtained with urine collected on different days of puerperium from 6 cases

Results with different days of puerperium from 6 cases						
Day of puerperium	Number of samples	Results with			Total number of samples positive	Remarks
		Untreated urine	Treated urine			
		Number of samples positive	Number of samples tested	Number of samples positive		
2nd	6	3	2	1	4	Some of the samples, negative with untreated urine, could not be examined by hormone extraction method as the quantity was small.
3rd	3	1	2	nil	1	
4th	5	2	3	1	3	
5th	6	1	3	nil	1	
6th	3	1	1	nil	1	
7th	1	nil	1	1	1	
8th	1	nil	1	1	1	
9th	1	nil	1	nil	nil	

might have been retained in the wall of the uterus.

Urine from non-pregnant women.—Samples of urine collected from healthy regularly menstruating women and those from males gave negative results both by treated and untreated methods and by the former method in doses 4 times that of pregnancy cases (equivalent to 200 mil. of untreated urine).

Reactivity of toads and intensity of reaction.—Up to a certain limit, there seems to be some positive correlation between the concentration of gonadotropic hormone in urine and the intensity of positive reaction as reflected by the number of sperms in the cloacal samples. In

positive samples, concentration of sperms as seen under the microscope varied widely from 'very abundant' to 'very scanty' as shown in table IV.

Other factors, besides the concentration of gonadotropin in urine which may possibly influence the intensity of reaction, are concentration of urine, age, health and nutrition of the toads, the season in relation to their breeding habit, and individual variations in reactivity. But concentration of urine does not seem to influence much the intensity of reaction; very dilute samples from early cases of pregnancy gave positive reaction graded as 'abundant' or 'moderate'. Health and nutrition of the toads

TABLE IV

Showing reactivity of toads and intensity of reaction

Type of urine (1)	Number of toads used (2)	Percentage of toads showing						Remarks (9)
		Very abundant (3)	Abundant (4)	Moderate (5)	Scanty (6)	Very scanty (7)	Negative (8)	
A. Untreated urine of :								
1. Early pregnancy	138	8.69	46.71	24.64	10.86	5.79	3.31	Figures under column (8) in- clude refractory, dead and mori- bund toads.
2. Late pregnancy	836	5.14	13.28	38.28	24.16	7.42	11.72	
3. Puerperium ..	78	2.56	15.36	10.24	61.84	
B. Treated urine of :								
1. Early pregnancy	6	..	33.33	66.67	
2. Late pregnancy	56	..	46.43	46.43	5.36	..	1.78	
3. Puerperium ..	28	17.86	14.28	..	67.86	

Very abundant = More than 100 sperms per field under high power.
 Abundant = 20-100 sperms per field under high power.
 Moderate = 5-20 sperms per field under high power.
 Scanty = 1-5 sperms in most of the fields under high power.
 Very scanty = 5-10 sperms in 20-30 fields under high power.
 Negative = No sperms seen.

no doubt affects their reactivity. Results with a few toads, starving for about a week, were very poor whereas healthy toads with the very samples of urine gave satisfactory response. Season does not seem to influence the reactivity of the toads but the authors hesitate to be emphatic on this point till further experience is gathered in mid-winter. Individual variation in reactivity is no doubt a factor but the percentage of such refractory toads is very low (about 3 per cent).

Variation in colour among male *B. melanostictus* is quite frequent, which may be due to differences either in nutritional or ecological factors. Observation of the authors is that earthy dark coloured male toads, with yellowish red colour over the skin covering the floor of the mouth and subadjacent vocal sacs, are very reactive. Experience enables them to pick up toads, 99 per cent of which turn out to be reactive.

Mortality among toads.—In the beginning, 9.26 per cent of toads put up for the test with untreated urine became moribund or died within 10 to 20 minutes after injection before giving positive reaction. With the addition of thymol (*vide supra*), the mortality came down to 3.29 per cent. The residual mortality might be due to pH of urine, individual susceptibility or elimination of metabolites, drugs or bacterial toxins in urine. It is apparent by comparative study with frog saline that the volume of urine injected is not responsible for the death. Individual susceptibility is no doubt a factor as it has been noticed, at times, one toad dying out of three injected with an equal quantity of urine from the same specimen.

Discussion

It is significant that most of the early cases of pregnancy, after the second week after the missed period, gave more intense reaction (i.e. 'very abundant', 'abundant' or 'moderate') whereas the reaction in majority of the cases in later half of pregnancy was less intense (i.e. 'moderate', 'scanty' or 'very scanty'). Some cases towards the end of the term gave 'false negative' results by untreated method while 4 days after delivery almost all cases became negative even by hormone extraction method. This signifies that the excretion and concentration of chorionic gonadotropin in urine is more in early months of pregnancy, particularly between 2 to 16 weeks after the missed period, than in the later months and it almost disappears from urine about 4 days after delivery. This is in conformity with the findings of Evans *et al.* (1937) and Browne and Venning (1936) who made quantitative study of urinary excretion of gonadotropin in pregnancy.

No 'false positive' result was recorded in the present series with urine for non-pregnant women and urine for males.

Of the various hormones tried to evoke this reaction in toads only chorionic gonadotropin of

pregnancy urine has been found to be successful. Equine gonadotropin and anterior pituitary gonadotropin have not yet been tried due to unavailability of the products locally. Although pregnancy urine gonadotropin is predominantly LH (lutemizing hormone), yet chemically and pharmacologically it differs from the LH of anterior pituitary. It also differs from equine gonadotropin which is mainly FSH (follicle stimulating hormone). It is not possible to pronounce any opinion without further study whether anterior pituitary gonadotropin and equine gonadotropin will give the reaction in toads as well. But whatever may be the final outcome of further study and elucidation, it is purely of academic interest and will not affect in the least the practical value and utility of this test because in human urine in pregnancy the question of equine gonadotropin does not arise and anterior pituitary gonadotropin is seldom present in any quantity in urine to evoke this reaction by itself.

Study with the standard chorionic gonadotropin of urine in pregnancy (unpublished work) convinces the authors that the minimum quantity to evoke this reaction is much less than what it is in the case of Hogben test which requires a minimum of 70 I.U. (Landgrebe and Hobson, 1949). Further, they have observed that the intensity of reaction runs parallel with the increase in dose up to a certain limit. This lends support to the authors' conclusion (*vide supra*) that 'within certain range positive correlation exists between the excretion and concentration of chorionic gonadotropin in urine and intensity of reaction'.

As mentioned before, one sample from a case of incomplete abortion gave negative result by untreated method which implies that the concentration of hormone in urine was low. The history of the case with the coming out of the products of conception along with decidua in the form of a cast lends support to the assumption that the moorings of the chorionic tissue in the wall of the uterus were severed a few days before the urine was collected, thus preventing further elaboration of the hormone and its entry into maternal circulation. In the meantime, the pre-existing placental gonadotropin in maternal body fluid might have come down to a very low level due to rapid elimination. Moreover, as discussed before, some specimens of urine towards the end of the term gave negative results by untreated but positive by treated method, which evidently was due to low concentration of hormone in urine. Towards the end of the term, placenta becomes senile with concomitant impairment of its function. This might be the cause of low concentration of hormone towards the end of the term. Viewed together, these two points lead to the conclusion that actively functioning chorionic tissue in biological continuity with the maternal tissue is necessary for satisfactory positive results.

Although there is no 'false positive' result in the present series of cases, its possibility cannot be entirely ruled out. Conditions other than pregnancy in which this hormone is present in urine in enormous quantities, *viz.*, chorionic epithelioma, hydatid mole and testicular teratoma, are likely to give strong positive results.

Besides, there are other conditions as menopause, castration in both sexes, genital carcinoma in women, certain benign tumours of ovary and pituitary, organic disease of the hypothalamus, tumour of adrenal cortex, etc., in which urinary gonadotropin content, either LH or FSH, rises appreciably. Whether the urine of such cases, which at times gives positive results with other biological tests of pregnancy, will show positive reaction with this test is yet to be seen.

During the progress of this work, the authors came across two more papers (Brody, 1949; Wiltberger *et al.*, 1948) reporting the suitability of *Rana pipiens* for the test. Other species of Ranidae and Bufonidae families are likely to be found suitable for this test. This will simplify the matter as to the availability of the test animal which can be had everywhere.

Summary and conclusions

1. Suitability of male toad, *Bufo melanostictus*, the common toad of India, in the biological test of pregnancy, based on the principle of Galli Mainini reaction, is reported.

2. In the present series of 308 samples from 143 cases of pregnancy, no 'false negative' result was obtained. With 92 samples of non-pregnant and male urine and frog saline, no 'false positive' result has been recorded.

3. Within a certain limit, a positive correlation exists between the concentration of the hormone in urine and the intensity of reaction.

4. In the first weeks of pregnancy and towards the end of the term, in some cases, the reaction has been found to be negative with untreated urine but positive by hormone extraction method, implying that concentration of hormone in urine is low during this period. The reaction becomes negative early in puerperium.

5. The distinct advantages of the test are its simplicity, inexpensiveness, rapidity and very high degree of accuracy. The result can be known within $\frac{1}{2}$ to 4 hours. The end-point is sharp and clear-cut. The test animal is available almost everywhere.

6. The same toads can be re-utilized every 10 to 12 days with proper feeding.

7. It is suggested that this biological test of pregnancy with various species of toads and frogs be termed as 'the Sperm Test of Pregnancy'.

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INCIDENCE OF ARTHRITIS IN SMALLPOX*

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ARTHRITIS as a complication of smallpox must be well known to all practising surgeons in India; but the literature on the subject is very meagre except an occasional reference to the effect that it does occur as a complication of smallpox.

The following observations were made during the 1948 epidemic in Calcutta and on 2,341 cases of smallpox admitted into Campbell Hospital. Total number of cases that developed arthritis was 10 and so the incidence rate is about 0.43 per cent. This appears to be rather insignificant but as we shall see presently it is really not so. Divided into different age groups, it was seen that out of the total of 2,341 cases, number of cases in the first decade was 115 and all the cases of arthritis belonged to that age group. As such the percentage that developed arthritis was 8.7 per cent which is quite a high figure.

It is admitted that compared to other surgical and eye complications, viz., pyemic abscess, osteomyelitis, erysipelas, conjunctivitis, corneal ulcer, etc., the incidence of arthritis is much less. Considering, however, the deformity this complication leaves behind in young growing children and the difficulties in treatment it subsequently presents to the surgeon, it is felt that it is one of the most serious complications and deserves more attention of the surgeons during the onset and course of the disease.

Following observations show that arthritis in smallpox presents sufficient peculiarities of its own, in incidence, clinical features and course of the disease, to get recognition as a special type of arthritis like tuberculous, gonococcal, syphilitic, etc.:

Age.—Between 4 and 10 years.

Sex.—More in females. Male to female ratio was 2 : 8 though the incidence of smallpox was nearly equally divided between the two sexes.

Site.—The commonest joint, as a matter of fact, the only joint affected in the present series was the elbow and it was more commonly bilateral. Seven cases were bilateral and 3 unilateral.

Onset.—It usually starts about 3 to 4 weeks after the onset of the disease. The type of eruption is always maculo-papular and discrete. No incidence has been seen in the confluent or other serious types. Arthritis starts usually after the eruptions have dried up and scales

started falling off, and the patients well on the way to recovery. The onset is acute with pain in the joint and moderate fever and if the affection is going to be bilateral, the other joint is affected within 3 to 4 days of the onset in the first one.

Course.—The temperature gradually rises and reaches maximum in 3 to 4 days' time. Toxaemia is never excessive. Joints are painful only when moved and not otherwise and even on movement they are not quite so painful as in acute septic arthritis. The joints are swollen partly due to effusion into the joint and partly due to periarticular inflammation. The condition may resolve or the joint may burst. When communication is established with outside, it is usually contaminated secondarily with staphylococcus. Cases, which resolve without any complication, run irregular temperature and settle down in about two weeks' time. The joint condition too settles down with temperature. Swelling and effusion subsides and pain gradually disappears. But limitation of movement persists particularly of flexion as joints are kept in extension during treatment. There is also some degree of limitation of pronation and supination of the forearm.

Blood picture.—Shows moderate leucocytosis, 8 to 10 thousand, with polymorphonuclears 68 to 75 per cent.

Joint fluid.—Aspirated fluid from joints in two bilateral cases was sterile on culture. Smear examination showed pus cells and no organism. Smear examination from three bilateral cases with discharging sinuses showed only staphylococcus, which probably was due to secondary contamination.

X-ray of the joint.—Commonest part to be affected is the head of the radius, next in order is the upper end of ulna and the least to be affected is the lower end of humerus. There is destruction of the epiphysis and epiphyseal cartilage and subperiosteal bone formation. The joint space is not obliterated and no bony ankylosis was noted in the present series.

An illustrative case note is given below:—

S. B. D., a female child, age 7 years, was admitted on 17th February, 1948, as a case of smallpox with history of 11 days' illness. The type of eruption was maculo-papular and discrete. The disease ran an uneventful course. The temperature settled down. The eruptions dried up and scabs started falling off, when on 3rd March, 1948, the patient complained of pain in the left elbow joint and on the next day had pain in the right elbow. The rise of temperature was gradual and in three days' time it reached the maximum. By that time the joints were swollen and there was effusion in them. The patient ran a low irregular temperature till 16th March, 1948, and then settled down and by that time the joint condition settled down too.

*Read at the Scientific Forum of the Campbell Medical School Reunion on 13th February, 1949.

TABLE III

Showing the chronic toxicity of carbamidophenylarsenious acid (C.P.A.) after 7 days' oral feeding.
Dose 4 mg./gm. daily

Day after start of drug feeding	C.P.A. 10 MICE			CONTROL (WITHOUT DRUG) 10 MICE		
	Group weight (gm.)	Average weight (gm.)	Mortality	Group weight (gm.)	Average weight (gm.)	Mortality
0	128	12.8	..	126	12.6	..
3	130	13.0	..	150	15.0	..
7	130	13.0	..	162	16.2	..
8	Drug stopped		
10	132	13.2	..	170	17.0	..
13	140	14.0	..	177	17.7	..
14	1/10
17	128	14.2
20	132	14.7	..	190	19.0	..
21	3/10
25	119	17.0	..	208	20.8	..
30	119	17.0	..	194	19.4	..

TABLE IV

Showing the comparative chronic toxicity of carbamidophenylarsenious acid (C.P.A.) and carbarstone under drug-diet administration for 15 days (10 mice in each group)

Week after start of drug feeding	C.P.A. GROUP				CARBARSTONE GROUP				CONTROL GROUP (NO DRUG)		MORTALITY IN GROUPS				
	1		2		3		4		5						
	0.5 per cent		1 per cent		2 per cent		2 per cent				1	2	3	4	5
	Group wt. (gm.)	Av. wt. (gm.)	Group wt. (gm.)	Av. wt. (gm.)	Group wt. (gm.)	Av. wt. (gm.)	Group wt. (gm.)	Av. wt. (gm.)	Group wt. (gm.)	Av. wt. (gm.)					
0	132	13.2	130	13.0	132	13.2	128	12.8	128	12.8
1st	150	15.0	148	14.8	125	12.5	146	14.6	163	16.3
2nd	160	16.0	156	15.6	144	14.4	175	17.5	181	18.1
3rd	168	16.8	158	17.6	152	15.2	189	18.9	203	20.3	..	1/10
4th	180	18.0	160	17.8	181	18.1	216	21.6	216	21.6	3/10
5th	180	20.0	168	21.0	147.7	21.1	213	21.3	215	21.5	1/10	2/10

Post-mortem findings of dead animals

All the animals dying after drug-diet feeding, as well as after 7 days' oral feeding of C.P.A., showed enlargement of liver with greyish infiltrations, uniformly distributed or in patches. In most cases, the kidneys looked pale and enlarged. Spleen was found to be slate-coloured in one animal under 1 per cent drug diet, while in others it was definitely enlarged. There was no peritoneal exudation or sign of acute intestinal congestion. Heart was always stopped in systole and showed no sign of enlargement or dilatation.

Post-feeding symptoms.—After a few days the character of the stools of animals having C.P.A. underwent a change. Though not liquid, the stools became light greyish in colour with semi-solid consistency. Sometimes greenish pigments were also noticeable in stools.

Moderate anorexia could be judged by the low intake of diet.

Pathology.—Liver, lungs, stomach, kidneys and heart of animals, dying after C.P.A. administration, were embedded in paraffin, after proper fixation, dehydration and clearing. Sections of 4 to 6 μ were cut by the Spencer's rotary microtome and were stained by the eosin-haematoxylin method.

Liver.—All the specimens from the chronic toxicity groups, which were examined, showed great disorganization of lobular structure, extensive degeneration of parenchymal cells and fatty infiltration inside the cell columns (as shown by non-staining vacuolated bodies). Portal capillaries were blocked by fibrin masses and fat globules. Scattered infiltration of leucocytes was present all over, specially around the portal vessels. Liver for acute toxicity

experiments (LD₅₀) did not show any gross abnormality.

Kidneys.—In acute toxicity tests, kidneys showed extensive hæmorrhages more in the descending tubular areas; glomeruli were congested, enlarged and packed with red blood cells and amorphous black masses, probably originating from the excretion of the drug. Tubular epithelium was degenerated in many places and the lumen of many descending tubules were found dilated and packed with R.B.C.

In chronic toxicity experiments, kidneys showed swelling of some tubular epithelial cells leading to obliteration of the lumen of some tubules and also complete degeneration of epithelial cells in some places.

Thickening of arteries was also seen.

Heart.—In acute toxicity experiments, heart did not show any abnormality. In 0.5 per cent drug (C.P.A.) diet it showed some thickening of pericardium with infiltration by leucocytes.

Spleen.—In acute toxicity experiments, extensive congested areas packed with R.B.C. could be seen.

Stomach and lungs did not show any gross abnormality.

Blood concentration of C.P.A. in mice

No other suitable method being available, Marshall's method (Marshall and Litchfield, 1938) was adopted after some modification for the estimation of C.P.A. Being a carbamidophenyl derivative, it was thought that acid might hydrolyse the carbamidophenyl group of C.P.A. to *p*-aminophenyl group. This could then be diazotized with sodium nitrite and coupled with alcoholic dimethyl- α -naphthylamine. Accordingly, some test experiments were carried with the compound mixed in blood, which showed beautiful colour reaction after hydrolysis of the protein-free blood filtrate with 2 N HCl for 1 hour and gave a proportionate variation within the range of concentration tested (1 to 15 mg.). A dose of 0.5 mg. per gm. was then fed orally to a group of 12 mice (20 to 22 gm.) and pooled heart's blood from 2 mice at a time was taken for estimation at intervals. The standard taken for the colorimetric estimation was a 5 mg. per cent solution of pure C.P.A. The standard solution was also similarly hydrolysed as the test samples. Table V gives the results of these experiments.

The above result shows that C.P.A. is fairly well absorbed from the gastro-intestinal tract, though its absorption appears somewhat erratic. The drug passes off from the systemic circulation at a fairly rapid rate, as shown by its disappearance in 5 hours' time. It is expected to be stored up in liver during its passage out of the system.

TABLE V

Intervals at which blood was taken (in hours)	Concentration of C.P.A. found (mg. per cent)
1	8.8
1	5.0
2	3.5
3	2.7
4	3.1
5	Nil

Effect of C.P.A. on red blood corpuscles

The drug was tested for any possible hæmolytic properties by keeping it in contact with washed 2 per cent suspensions of guinea-pig red blood corpuscles for 24 hours at room temperature. No change in the oxygenating capacity of the cells was noticed. The supernatant liquid, after complete settlement of the corpuscles, was found to be free from any trace of hæmolysis.

Discussion

From tables I to V it is evident that, when compared with carbarsone, *p*-carbamidophenylarsenious acid (C.P.A.) is a more toxic drug. While a dose of 1 mg. per gm. daily for 2 days is apparently tolerated, 2 mg./gm. dosage gives rise to late mortality. Under drug diet as well as after oral feedings for seven consecutive days, late mortalities were encountered generally from the third week onwards. Orally, 4 mg./gm. dosage gave 30 per cent mortality, while even 0.5 per cent drug diet of C.P.A. caused some mortality. Carbarsone even in 2 per cent diet caused neither any mortality nor any reduction in the progress of normal growth of animals. Retardation of growth during the period of drug feeding of C.P.A. was very well marked. When the drug administration was stopped, the animals, however, tried to regain the lost weight, though unable to cope with the control group of animals (figure II). The retardation of growth appeared to be caused by the specific effect of the drug as well as by the production of a fair amount of anorexia.

The gross post-mortem findings and histological examination of tissues of dead mice suggest that liver and kidneys probably take the brunt of the first attack by the drug (C.P.A.). Though the intestinal tract did not show any gross lesion, yet, from the consistency of the stool of drug-fed animals, it could be opined that definite irritation of the gastro-intestinal tract did occur. With carbarsone group and the normal control groups no apparent physical changes occurred, showing thereby that carbarsone is a far more tolerated drug.

Summary

1. The acute and chronic toxicity of *p*-carbamidophenylarsenious acid (C.P.A.) has been studied in mice. Comparison of chronic toxicity has been made with carbarsone,

2. C.P.A. is being found to cause retardation of growth and late mortalities in mice even in as low a strength as 0.5 per cent drug diet.

3. C.P.A. appears to be a more toxic drug than carbarsone.

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A Mirror of Hospital Practice

TWO CASES OF VESICULAR (WEEPING) ECZEMA TREATED WITH ANTI-HISTAMINIC DRUG

By P. C. SEN, L.M.P.
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1. AN adult male had a superficial negligible injury over his abdomen by a rusted blunt weapon. No immediate aseptic precaution was taken. Within 2 or 3 days, there appeared minute vesicular eruptions around the wound, which went on spreading rapidly. This made him take the help of a doctor, who gave him sulphonamide dressing, and sulphathiazole by mouth. Instead of improving the eruptions went on spreading rapidly and had covered almost the whole of abdomen, arms, legs and even the face.

The eruption appeared as minute papules which later became vesicular and itched. They coalesced, and on breaking up and drying formed crusts over themselves. There was always a serous sticky secretion oozing from them, and whenever they came in contact with healthy but scratched skin, they produced the same pathological state.

At the first sight they suggested bacteria as the causative factor, and penicillin as the treatment. Accordingly, penicillin was given every 3 hours, first 4 injections 50 thousand units each, and the subsequent 12 injections 25 thousand units each. But this antibiotic drug gave a very disappointing result; instead of improving the eruptions went on spreading. Consequently penicillin was stopped and anti-histaminic drug (Antistine tablet, Ciba) was given, one tablet three times a day by mouth, and Goulard's lotion with calamine 2.0 dr. to a pint, for external application. It was really surprising to note that such a spreading disease was brought under control by the second day, and from the

third day, nearly half the eruptions had dried up. At some places the itching and dermatitis persisted. Nupercainol ointment (Ciba) completed the cure.

2. A young girl had an eruption over her neck, which had an erysipelatous look. Considering this to be erysipelas, the attending physician started penicillin injection, 50 thousand units per dose every three hours, and had continued for 60 hours. The eruption instead of showing any amelioration went on spreading very rapidly, and had covered the whole body excepting the palms, soles and the head. The face and several other portions of the body had swollen so much as to give a horrible look. There was a little rise of temperature too.

The character of the eruption was the same as in case no. 1. It first appeared as minute vesicles with itching. These on breaking up coalesced discharging sticky serous secretions which, on drying, formed crusts. The secretion on coming in contact with the scratched healthy skin produced the same pathological state, and had a tendency to spread very rapidly.

Antistine tablets, one 3 times a day, were given by mouth, and Goulard's lotion with calamina preparata was given for external application. In this case also the disease was found to have been controlled on the second day and from the third day desquamation went on rapidly.

Both the cases, as one's teachers taught one, must be called vesicular (weeping) eczema. In former days, Goulard's lotion with calamine used to cure them, but took a very long time. That such a widespread pathological condition of the superficial layer of the skin can be produced by allergy is beyond conception. The points showing that it was not a lesion produced by any virulent organism were: (i) no lymphatic gland was found involved and (ii) no constitutional symptoms, such as fever, rapid pulse and prostration, were present. The slight temperature in the second case was quite negligible in comparison with the area involved.

One must admire these anti-histaminic drugs. They are working like magic just as the anti-biotic drugs are doing.

Occasional Notes

THE PLACE OF CLINICAL PATHOLOGICAL MUSEUM IN MEDICAL EDUCATION

By P. N. WAH, M.D., M.R.C.P. (Lond.)

and
 K. C. SAMUEL, M.D., B.S.

(From the Department of Pathology, Medical College, Agra)

THE pathological museum is a necessary adjunct to any well-equipped medical college

and, as the years go by and knowledge grows, it must play an increasingly important rôle in medical education. It should succeed in illustrating in a clear and instructive manner the causation of human disease, the underlying pathological changes, and the methods of prevention and treatment. Therein lies the great educational value of the teaching museum, which is in effect a sumptuously illustrated textbook. A student may learn more from a quiet hour spent in such a museum than he is likely to do from any ordinary routine lecture. Museum study should form a definite part of the medical curriculum, a sequel to lectures, ward clinics, and laboratory and post-mortem demonstrations. With the increase of specialized teaching, it is essential for the student to have some centre where he can view the subject as a whole. Such a centre is provided by a well-arranged clinical pathological museum.

Every one who is engaged in teaching of pathology has a museum of some sort, to which he can refer in illustrating the lectures. A pathological museum is commonly regarded as a collection of specimens of gross disease. These vary from traditional old collections of pickled specimens stored in various assorted bottles, absolutely unattractive and uneducative to such superb collections of rare and instructive materials as those of the German universities, the London hospitals, and the Royal Colleges of Surgeons of London and Edinburgh. Admittedly these have played a part in their time and still do so. But the concept of pathology has undergone gradual evolution from the pathology of pathologic anatomy of Rokitsansky, through the adoption of procedures of physiology and chemistry by Virchow and Cohnheim, and incorporation of methods of bacteriology, parasitology and immunology following Pasteur, to the present position when teaching of pathology centres round the living patient. It is to be regarded as having a functional as well as an organic side concerned with the production of clinical pictures as well as the lesions. The idea of teaching pathology, therefore, should be to make the subject an exposition of cause, processes and results of disease. With this in view, clinico-pathological correlation should be a major aim in teaching. Hence the museum should be wider in scope, the object of which is to display besides the gross specimens, the microscopic, clinical and radiological aspects of disease. In addition, this presentation of more than one aspect of the subject makes it more attractive and interesting for the students.

Those who visit the Wellcome Medical Museum in London, Army Medical Museum at Washington, Boyd's Museum at Best and Benting Institute at Toronto and the scientific exhibits section at the meetings of the American Medical Association or the American Association of Pathologists and Bacteriologists will see these ideas embodied in them.

The means by which these objectives may be attained will vary to a great extent with the individual worker. We at the Agra Medical College have of late completely transformed the museum along these lines. The most important single feature has been the introduction of pictures, charts and models interspersed with the specimens. These represent clinical histories, gross and microscopic findings, temperature charts, chemical pathology, skiagrams, electrocardiographic tracings, various clinical states, animal parasites and their life cycles, bacteria and the lesions caused by them, skin diseases, eruptive fevers, diseases of eye and throat, illustrations of what is seen with the ophthalmoscope, bronchoscope, sigmoidoscope, cystoscope, etc., and photographs of masters of medicine.

As an illustration, we may take a few examples. In the section on cardiology, in addition to the specimens of heart showing mitral stenosis, there is a chart giving the clinical history of a typical case, x-ray picture showing the characteristic changes in mitral stenosis, electrocardiographic tracings in such a patient, a clay model showing clubbing of fingers, a painting showing cyanosis of lips and tongue and a picture of Harvey explaining his doctrine of circulation to Charles I. Hypertension is illustrated by clinical history of a case of hypertension, x-ray of enlarged heart, electrocardiographic tracings with left-sided preponderance, microphotograph showing kidney changes of nephrosclerosis, coloured slide showing the fundus appearance, and specimen of hypertensive heart. Coarctation of the aorta is illustrated by diagrams of collateral circulation, roentgenograms of the heart and grooving of the ribs caused by enlarged internal mammary arteries, electrocardiographic tracings and a picture of Dr. Maude Abbott.

In the section on protozoology, malaria is illustrated by pictures showing the life cycle of the malarial parasites in man and in the mosquito, the anopheles mosquito compared with the eulex, the clinical histories of tertian, quartan and malignant malaria, temperature charts, pictures of blood films showing various stages of parasites, the parasites in the brain, and the pigment in the spleen. In the section on helminthology, ankylostomiasis is illustrated by a clay model of hookworm, mounted specimens of the male and female worms, specimen of the intestine with the *Ankylostoma duodenalis* attached to the mucous membrane, diagram showing the life cycle of hookworm, specimens of *Necator americanus* (male and female) and the comparative diagrammatic illustration of *Ankylostoma duodenalis* and *Necator americanus*.

X-rays have proved a valuable adjunct in illustrating the disease as a whole. Alongside the specimens of bronchiectasis or cavitation in the lung, the student sees the lipiodol picture of the former and a cavity in the latter. Amongst the

many lesions which are well illustrated by radiograms are gallstones, renal stones, hydro-nephrosis, bone lesions and the distortion of the cerebral ventricles by space occupying lesions of the brain. Electrocardiographic tracings have been included in the section on cardiology.

Temperature charts are used where the fever forms a characteristic finding of the clinical picture, as in pneumonia, typhoid, malaria, kala-azar, Hodgkin's disease, and eruptive fevers.

Models have been found of the greatest value in diseases of the skin and eye. Actual apparatus has been displayed in the section on chemical pathology.

'Composite picture' illustration has proved a very useful method of teaching bacteriology, parasitology and hypovitaminosis. Clinical, pathological and bacteriological features are combined in one frame. In the composite picture of typhoid fever, one sees the microscopic appearance of typhoid bacilli, the characteristic growth on culture media, typical biochemical reactions, temperature charts, intestinal ulcers, early and late microscopic changes in the Peyer's patches with the characteristic macrophages. The echinococcus infection is illustrated by pictures showing the morphology and life history of the worm, hand drawings of eggs, schema of hydatid cyst in liver and diagnostic methods. Interspersed in between the pictures are the written descriptions. The lesions caused by deficiency of vitamin-B complex taught by composite picture comprising of the chemical formula, determination methods, daily requirements, natural sources, and pictures of rats with polyneuritis developed on vitamin B₁ deficient diet, B₂ deficiency dermatitis, pellagra, beri-beri and α -ray of dilated heart.

Single pictures have been found to be very useful in diseases of the eye as the appearance of fundus in various conditions. For diseases of the blood, as in pernicious anæmia, we have pictures of the characteristic blood films, of reticulocytosis, of normoblasts, megaloblasts and gross and microscopic appearance of hyperplastic bone marrow. This is further supplemented by a specimen of liver with prussian blue reaction showing deposits of hæmosiderin. Pictures of masters of medicine are of singular value in inspiring the students. The section on kidney diseases is illustrated by a picture of Richard Bright, and that on the heart by pictures of Harvey and Maude Abbott. Brain tumours have Cushing and Cajal. Anæmias have Thomas Addison. Section on tuberculosis include portraits of Laennec and Koch, while that on syphilis includes Schaudinn, Ehrlich and Wassermann. Bacteriology is towered by Pasteur.

In Agra, the teaching of pathology is divided between two years. In the third year the students study general pathology as retro-

gressive processes, inflammation, circulatory disorders, tuberculosis, syphilis, neoplasms and general bacteriology, etc. In fourth year pathological processes in individual systems are considered. The museum which is housed in two stories is accordingly divided into two sections—one on general pathology and the other on special pathology. The third year students use the former while the fourth year use both the sections. In the section on general pathology, composite representation of disease is the method adopted for teaching. For example, the section on tuberculosis contains specimens and pictures of tuberculous lesions of the lung, kidney, lymph nodes, bone, bowel, pictures of the human and bovine type of tubercle bacilli, in smears and culture, post-mortem appearances in guinea-pig after inoculation and pictures of tuberculin reactions.

Final year students also have classes in applied pathology in the museum. The teaching here is done by the clinicians and the aim is clinico-pathological correlation. With the same object in view small hospital museums in different wards consisting of common pathological specimens, clinical photographs, charts and paintings are being provided at Agra. These prove handy for purposes of teaching in the wards and will lessen the necessity and obvious undesirability of shifting specimens from the main museum.

So much for the general arrangement and the ideas which have served as guiding principles in the making of the museum. A few words about the method of display are necessary. In almost all the museums the specimens are kept in rectangular or round jars arranged on horizontal shelves which may be open or closed. This is not an ideal arrangement because jars horizontally placed are not best suited for purposes of studying. The best display of specimens that can be seen is in the Boyd's Museum at Toronto University. Here the specimens are mounted in watch glasses and narrow glass cells, and it is remarkable how large a specimen the largest size watch glass will accommodate. Besides, these are much cheaper than the jars. The watch glasses are placed on stands constructed in the form of a reading desk. These usually contain three sloping shelves, the centre one being on a level with the eye of the student sitting on a stool in front. This affords the natural position in which a book is held to be read. Pictures, charts, etc., are also placed in the sloping position. His display of α -ray films is also very attractive. This is done by a combined film cabinet and viewing box. The upper half is closed and the lower open. The films are mounted in light wooden frames which can slide up and down. When the wooden frame containing films is in use, it is lowered in front of a pane of ground glass and illuminated by fluorescent

PLATE XII
INCIDENCE OF ARTHRITIS IN SMALLPOX ' R N. CHATTERJEE.
(O. A) PAGE 49



CAMPBELL HOSPITAL
17A48X102
X-RAY DEPT CALCUTTA

Fig 1

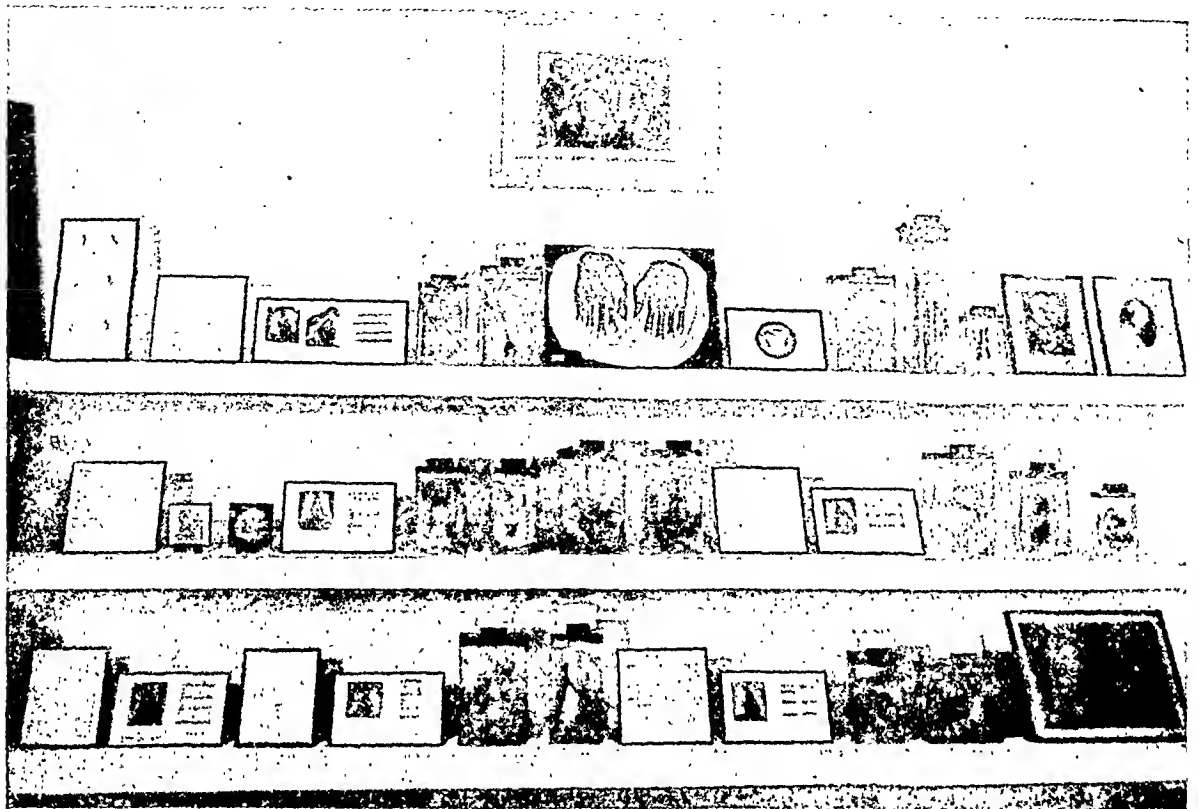


Fig. 1.

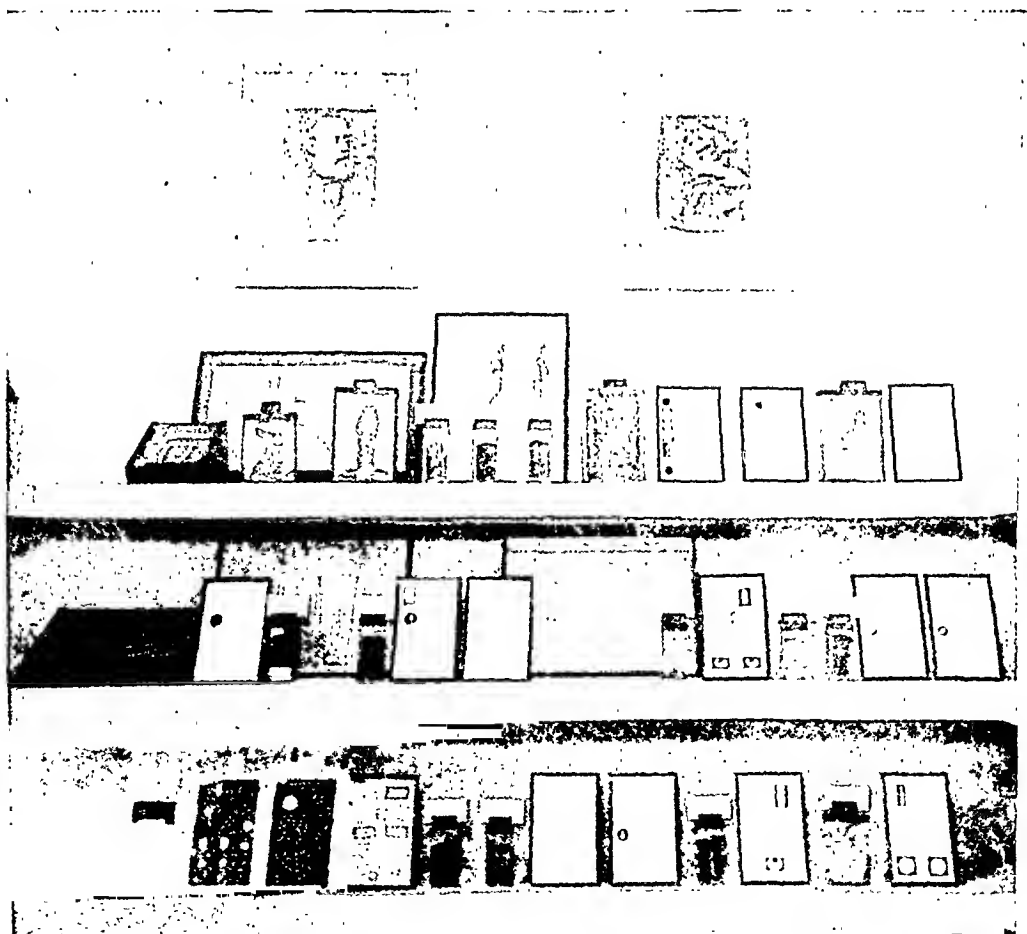


Fig. 2.

light. When the frame is not in use, it is raised into the upper half of the box and secured by a sliding bolt. Similar boxes have been used in Boyd's Museum for transparencies of clinical pictures, microphotographs and painting of blood pictures on transilite films.

The method of cataloguing is also important. At Agra, it is a combination of short descriptive labels and the full length catalogue giving the clinical histories, gross and microscopic description of each specimen. We are firmly convinced regarding the value of this method. As the spare moments of the student are few, any system which is fatiguing will probably fail to keep his attention. To place a number on a jar referring to a catalogue of which there is often one copy, is sure way of neutralizing any value the museum may otherwise possess. The catalogue is printed and most of the students have their personal copies.

Thus a good museum containing mounted and unmounted specimens microscopic slides, microphotographs of the representative findings, clinical histories, pictures, charts, models and bibliography is a definite asset. Still there is hardly any museum worth the name in most of the colleges in the United States. To maintain such a museum up to date, a separate staff is necessary and this plus the constant changing of preservatives and glass jars entails large expenditure. Besides, the space requirements for display and storage purposes of mounted specimens is formidable. Instead the American colleges are concentrating on pictorial museums consisting of photographs, kodochromes and black and white pictures of the gross as well as microscopic findings. These are all indexed. The slide material, besides being available in the museum, is projected in class lectures, clinico-pathological conferences, etc. The most impressive museum of this kind can be seen at the department of pathology, St. Luke's Hospitals, Chicago, Ill., organized by Dr. Edwin Hirsch. The essential requirement for making such a museum is a good photographic department. We feel that such a museum has a much more teaching value.

However, almost all the colleges have some sort of museum and so long as it is not possible to make a good pictorial museum, it is but fair that the existing pathology museums should be turned into clinical pathological museums. These represent an attempt to illustrate in graphic form for the student the correlation of gross and microscopic lesions with clinical and x-ray findings, which, in Agra, we have found useful in teaching not only of pathology but also medicine and surgery. Even the clinicians are coming to realize that the museum is a storehouse of information and much more teaching by them is done in the museum now than ever before. They have realized that it is a museum of disease and not merely of pathological specimens.

Such a museum has unlimited possibilities and it may be made the centre of teaching not only for undergraduates but also for those preparing for higher examinations. As Robertson remarked 'it may thus be possible to elevate the stone that has been almost rejected to become the head of the column' (see figures 1 and 2, plate XIII).

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Therapeutic Notes

NOTES ON SOME REMEDIES

XXXII.—DEHYDRATION AND ITS TREATMENT

By R. N. CHAUDHURI, M.B., M.R.C.P., T.D.D.

Professor of Tropical Medicine, School of Tropical Medicine, Calcutta

Part IV. Dehydration in Infants

Water metabolism in infants

A NEWBORN infant's body has 80 per cent by weight of water against 70 per cent in the adult, and a much larger proportion of that water is extracellular than in the adult. For its weight the infant requires much more water than the adult, its daily requirement being 150 ml. per kg. (about 2½ oz. per pound) against 50 ml. per kg. for the adult. The infant's loss of body water is also greater, being at the rate of 4 per cent of its weight per day against 2 per cent in the adult. It is therefore evident why infants ingest so much more water than do adults in relation to their body weight and why they withstand dehydration badly. Furthermore, owing to their relatively greater metabolism, there is greater loss of water by vaporization through the lungs and skin, and a somewhat less than half the water intake is available for renal excretion. If the extrarenal losses are increased by fever, hyperpnoea, vomiting or diarrhoea, the water available for the kidneys may be too low for excretion of waste products. The infant kidney is unable to concentrate solids in the urine to the same extent as an adult one can. So as soon as urinary output falls the blood urea rises. As the infant kidney is

also not efficient in concentrating salts oedema may easily be produced when normal saline injections are given to relieve dehydration. This is particularly the case with premature babies whose urea and mineral clearances are lower than in normal babies, and with babies fed on cow's milk as it contains more salt. The important point is to note that the trouble from dehydration arises from too little water being available for excretion and that an infant needs extra water (and salt in some cases) whenever the output by the skin, lungs and bowel is increased.

Principles of treatment

The most important single factor in treatment is the relief of dehydration, and this must be given quickly as irreversible changes set in earlier than in adults. Enough water must be given to replace what has been lost, and in addition enough for the infant's normal requirements to enable the kidneys to function efficiently. The lost salt must also be replaced, remembering that there is danger in giving too much salt or too little. As an infant can rarely excrete urine containing more than 1.4 per cent of salt, injections of normal isotonic saline may easily lead to oedema. On the other hand, it is not possible to relieve dehydration associated with salt deficiency without giving enough salt, and if large volumes of simple glucose solution are given, there is risk of water poisoning (Young, 1943).

In dehydration, the infant's water and salt requirements need to be assessed as carefully as in adults, but the criteria given for the latter (*I.M.G.*, September 1949, p. 396) cannot be applied to infants. A good deal depends on clinical judgment and practical experience, but as a rough guide, it is sufficient to calculate the daily requirements of a baby of one year and under at the rate of $2\frac{1}{2}$ oz. per pound of body weight and add 5 to 10 oz. according to its weight and the degree of dehydration. Thus a baby of 15 pounds with a moderate loss would require about 37 oz. plus 7 ounce, i.e. 44 oz. of fluid in 24 hours. But it is better not to give more than 20 oz. (600 cc.) in 24 hours intravenously to an infant under 6 months of age.

Fluid used

A mixture of normal saline and 5 per cent glucose in equal parts should be used to make up the fluid loss, and this is followed by a maintenance infusion of one-fifth normal saline, that is 1 part of normal saline to 4 parts of 5 per cent glucose, to supply the daily needs. If diarrhoea or vomiting has been very profuse, it may be necessary to give some normal saline at the start. Another solution that is commonly used is Hartmann's solution (Ringer-lactate). Its composition being as follows :

	(Approx.)
Sodium chloride	.. 6.0 gm.—1½ dr.
Potassium chloride	.. 0.4 gm.—6 gr.
Calcium chloride	.. 0.2 gm.—3 gr.
Sodium lactate	.. 2.7 gm.—40 gr.
Aqua	.. 1,000 ml.—33 oz.

The chlorides are those present in normal plasma in roughly their normal relative amounts, and the lactate has been added to combat acidosis to which children suffering from dehydration are so liable. The presence of acidosis is indicated by respiration of air-hunger type and drowsiness. Some authorities consider that there is no advantage in adding the sodium lactate (or sodium bicarbonate), as the kidneys in most instances can restore the general electrolyte equilibrium to normal, provided that sufficient water is available for adequate renal excretion. In an acutely dehydrated child who is usually in shocked condition, it is essential to give plasma or serum in addition to saline.

Methods of administration

Fluid is given by mouth, and even when a child is vomiting, small sips can be given at frequent intervals. This can be supplemented by rectal administration when the patient has no diarrhoea, but this route is not suitable for children under the age of 3 years. The gastric drip (the tube being passed *via* the nose into the stomach) may be very helpful especially for the immature babies.

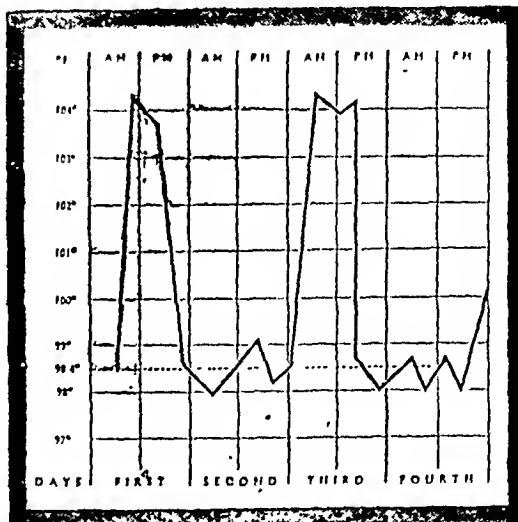
The intravenous route is frequently the only one by which the depleted fluid can be restored sufficiently quickly; it is given by continuous drip or, if this is not possible, at 4 to 6 hourly intervals. In certain circumstances, the subcutaneous or intramuscular method may have to be adopted. The intraperitoneal administration has the advantage in that a greater quantity of saline can be given more speedily than by the other methods, and absorption is also quicker than from the subcutaneous tissues. To give the injection the bladder is first emptied, then the abdominal wall is picked up off the intestine, and the needle is inserted slantwise in the middle line. Five to ten ounces are then allowed to run by gravity into the peritoneal space. If given in moribund stage, the fluid may not be absorbed at all and for obvious reasons the operation is not entirely without risk.

Progress

The adequacy of treatment can be judged from general improvement and amount of urinary output, but in infants it is not always possible to measure the latter though it can be roughly guessed from the wet linen. Daily weighing of the patient is helpful. The change in weight is a much more sensitive indicator of the water balance than estimation of serum chemistry (Young).

Further details of treatment will be given in the next article.

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the treatment of malaria



Temperature chart of benign tertian malaria

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value than was previously thought, while other independent tests have demonstrated that BOVRIL promotes a greater flow of gastric juices than any of the other gastric stimulants used in the tests.

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Indian Medical Gazette

FEBRUARY

PLEASANT 1949-50 WINTER IN CALCUTTA AND ASSOCIATED CONSIDERATIONS

LAST summer we enjoyed a pleasant weather in Calcutta and correlated it with an unusually large number of Nor'westers. Another correlation, unfortunately, could be the visitation of plague (Editorial, 1949a).

This winter has been equally enjoyable and we are putting on record the meteorological data, for the months of December 1949 and January 1950, kindly supplied to us by the Director, Regional Meteorological Centre, Alipore, Calcutta, at our request. Two previous winters have been included for comparison.

One conclusion emerges: the relative humidity has been low during this winter.

Attention has been drawn to the importance of relative humidity by climatologists and air-conditioning experts within recent years. Low relative humidity makes winters in cold and temperate zones intolerable but in the tropics pleasant. For conditioning air for comfort in the tropics, however, the experts appear to be undecided. For a given 'effective temperature' one school favours low temperature with high humidity and another a higher temperature with low humidity (American Society of Heating and Ventilating Engineers, 1943).

Calcutta has benefited from the second combination. Of all indices of comfort, be they based on physical instruments, 'effective temperature' or 'operative temperature' (Newburgh, 1949), the one based on the dry and wet bulb is the easiest to comprehend and adjust in the humid regions of the tropics. It appears that our cooling and ventilating engineers in Calcutta need not have a divided opinion on the matter.

The difference between the dry and wet bulbs, which depends on the relative humidity, is obviously much more important than the mere maximum or minimum reading. The wet bulb 'feels' the cold (or the coolness in the tropics) like human beings. The wind, so material between comfort and discomfort in colder regions, does not make much difference in places like Calcutta except when it is associated with Nor'westers in the summer.

The Calcutta pleasant winter may be correlated with the cold wave which later swept over nearly the whole of India, or may of course be linked with the recent changes in the sun spots. (The cold wave, incidentally, is a

regular occurrence which usually remains confined to the more northerly regions of Asia. This year it has strayed southwards.) The general mitigation of the tropical summer conditions all over the country last year may be correlated with polio which has recently attracted attention in India (Editorials, 1949b, 1949c).

Obviously a pleasant cold weather was frequently operative for quite 5 months in the gaiety of Calcutta of olden days. Here is an advertisement from the daily press of 75 years ago.

(Advertisement)

CALCUTTA THEATRICAL SEASON 1875-76

Mr. English begs to announce to the Public of Calcutta that he has made arrangements to open a Theatre in Calcutta for a season of not less than twenty weeks, commencing in October next; during which season he intends, with some of his present Company and several new Candidates for the approbation of the patrons of the Theatre, to produce the latest Novelties that he can procure in England, Paris and America, including COMEDY, DRAMA, BURLESQUE, FARCIE and OPERA BOUFFE.

From the *Statesman* of 27th February, 1875.
(*Daily Press*, 1950.)

According to a recent review of the situation in Europe the grandfather is right in his impression of the weather. Modern research agrees that the cold months are getting less cold. Fauna and flora from southern regions are moving northwards. Glaciers are retreating. In Africa lakes are drying up and the Sahara spreads year by year. In 25 years Britain may have the Riviera climate (Morley, 1950).

An occasional severe winter in Europe is looked upon as a freak of nature.

Whatever be in store for India, in matters of bodily comforts, much attention to matters meteorological will be necessary, for matters of health, with the approaching industrialization of the country. The need for the increased attention is obvious from occurrences like the unusual Smog Episode in Donora, Pa., located on the Monongahela River in Washington County, Pa., about 30 miles south of Pittsburg (Schrenk et. al., 1949).

'During the last week of October 1948, a heavy smog settled down over the area surrounding Donora, Pa. Weather men described it as a temperature inversion and anticyclonic conditions characterized by little or no air movements, prevailing over a wide area encompassing western Pennsylvania, eastern Ohio, and parts of Maryland and Virginia. This prolonged stable atmospheric condition was accompanied by fog and permitted the accumulation of atmospheric contaminants resulting in dense smog particularly in highly industrialized areas. . . . It was reported that steamers of carbon appeared to hang motionless in the

TABLE

Station—Alipore, Calcutta

Month and Year—December 1945

Date	At 8 hours I.S.T.		At 17 hours I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	Relative humidity, per cent		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				8 hours I.S.T. °F.	17 hours I.S.T. °F.	
1	64.8	61.8	73.0	65.1	81	59	1	84	63	Nil
2	62.7	61.0	72.5	61.2	83	59	1	91	49	"
3	62.9	57.8	71.7	61.7	83	55	1	72	54	"
4	62.0	57.2	71.7	61.0	80	55	1	73	52	"
5	56.9	54.1	69.2	59.8	79	54	2	81	54	"
6	56.3	55.2	71.3	61.3	80	54	1	93	53	"
7	61.4	57.4	71.8	62.0	79	54	1	77	55	"
8	61.4	58.0	72.0	63.2	79	57	2	80	59	"
9	61.0	57.7	71.0	61.9	79	58	2	77	58	"
10	62.2	58.0	73.0	63.3	80	57	2	77	56	"
11	61.2	56.4	70.1	61.1	79	58	3	71	57	"
12	62.1	56.8	73.4	62.0	79	59	3	71	49	"
13	63.0	57.0	72.3	64.0	79	56	2	67	61	"
14	65.0	59.0	74.1	67.4	81	62	2	68	70	"
15	63.0	59.8	68.1	62.4	79	59	2	62	72	"
16	61.8	56.0	73.9	61.3	72	60	3	66	42	"
17	38.1	56.8	71.8	61.3	79	55	4	63	52	"
18	58.4	52.8	71.6	60.9	78	55	3	67	51	"
19	59.0	53.5	71.0	61.0	78	55	3	68	53	"
20	58.2	54.3	70.1	59.6	80	53	1	76	50	"
21	56.5	52.5	71.8	59.4	78	51	1	75	45	"
22	54.0	52.7	72.0	61.7	77	51	1	90	53	"
23	59.7	58.7	72.7	63.0	81	54	1	94	46	"
24	60.3	52.1	66.7	58.2	83	57	1	55	57	"
25	58.0	49.3	67.0	55.6	75	51	2	75	43	"
26	49.0	48.0	67.7	57.4	73	47	1	93	50	"
27	53.2	52.2	69.5	60.5	75	50	1	93	56	"
28	59.3	56.5	73.0	64.3	77	53	1	82	60	"
29	58.8	57.0	71.0	63.0	79	57	2	88	62	"
30	58.0	53.5	67.4	56.5	75	55	..	73	46	"
31	54.0	49.8	66.2	54.2	73	50	4	74	41	"

TABLE—*contd.*

Station—Alipore, Calcutta
Month and Year—January 1946

Date	At 8 hours I.S.T.		At 17 hours I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	RELATIVE HUMIDITY, PER CENT		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				At 8 hours I.S.T.	At 17 hours I.S.T.	
1	51.2	48.8	68.2	57.9	72	48	2	61	50	<i>Nil</i>
2	52.0	50.0	68.6	55.8	75	49	2	86	39	"
3	50.0	49.0	70.1	58.9	75	47	1	93	47	"
4	56.6	51.6	69.0	55.8	77	51	2	69	38	"
5	56.2	52.6	70.5	59.0	76	54	2	73	47	"
6	58.1	52.5	70.7	59.0	77	54	2	67	46	"
7	57.8	52.0	71.6	60.6	77	55	3	46	50	"
8	58.6	53.4	71.5	61.2	78	56	2	69	52	"
9	58.3	54.3	71.3	63.0	78	55	2	76	61	"
10	55.9	54.9	72.0	62.7	78	54	1	93	57	"
11	57.0	56.0	74.8	62.8	78	55	1	94	48	"
12	57.3	55.3	72.7	60.0	81	56	1	87	44	"
13	56.5	54.3	73.5	60.5	79	52	2	86	43	"
14	55.2	54.8	73.8	62.3	79	54	2	97	49	"
15	55.8	55.2	74.7	62.3	79	54	1	97	46	"
16	55.9	55.0	76.2	64.2	82	54	1	93	49	"
17	61.2	60.7	76.6	66.8	85	56	1	97	58	"
18	60.2	59.7	78.5	67.0	83	59	1	97	52	"
19	63.3	59.6	77.8	67.4	86	60	1	80	56	"
20	59.3	57.8	76.4	64.7	84	57	1	91	50	"
21	54.9	53.9	75.0	60.3	82	53	1	93	38	"
22	55.3	53.5	75.4	59.9	80	53	1	87	35	"
23	56.1	54.3	76.2	62.3	81	55	1	87	41	"
24	58.4	57.2	78.8	66.6	82	56	1	93	46	"
25	58.5	57.5	82.2	65.1	83	57	1	94	36	"
26	59.0	57.6	81.6	62.6	87	57	1	91	30	"
27	58.8	56.8	81.7	62.4	87	56	1	88	29	"
28	58.6	56.6	80.7	64.2	87	57	2	88	37	"
29	63.2	54.2	79.0	60.0	86	58	2	52	27	"
30	56.3	52.3	79.0	61.3	82	53	2	75	31	"
31	57.7	52.5	81.3	63.3	88	53	2	70	32	"

TABLE—contd.

Station—Alipore, Calcutta

Month and Year—December 1948

Date	At 8 HOURS I.S.T.		At 17 HOURS I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	RELATIVE HUMIDITY, PER CENT		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				At 8 hours I.S.T. °F.	At 17 hours I.S.T. °F.	
1	62.3	61.8	70.4	63.3	73	58	1	97	66	Nil
2	64.3	60.7	71.0	64.0	76	59	2	81	66	"
3	64.4	60.0	71.1	64.0	76	60	2	75	66	"
4	66.0	61.0	72.0	61.6	78	62	2	74	65	"
5	67.0	61.1	72.0	65.0	78	61	1	61	59	"
6	66.7	63.0	71.7	65.3	79	59	1	81	69	"
7	65.0	63.0	71.2	64.7	80	59	1	89	60	"
8	66.1	62.6	72.2	65.0	79	59	1	81	67	"
9	64.0	60.7	70.0	62.0	78	58	2	82	61	"
10	65.0	59.0	69.0	60.0	78	59	2	68	56	"
11	62.0	58.8	69.0	60.0	77	55	2	82	56	"
12	64.2	58.7	70.0	60.5	77	55	1	70	55	"
13	61.0	54.1	69.2	58.0	76	55	2	61	46	"
14	62.2	54.8	70.0	62.0	76	56	4	59	61	"
15	62.0	58.0	71.7	63.0	78	57	2	77	62	"
16	61.1	59.0	70.0	63.0	80	55	1	88	66	"
17	57.9	56.8	69.3	63.0	79	54	0	94	67	"
18	63.5	60.0	73.0	65.0	77	57	1	80	63	"
19	62.5	59.5	71.9	62.0	79	58	1	83	54	"
20	61.0	57.5	70.0	62.0	78	55	2	80	61	"
21	63.0	58.8	70.0	61.0	77	55	2	78	57	"
22	60.0	59.0	71.0	63.0	76	54	1	94	62	"
23	61.0	59.0	73.0	61.0	77	55	1	88	47	"
24	58.9	56.0	73.0	60.3	80	54	1	82	45	"
25	56.0	54.5	72.0	60.6	79	53	1	90	48	"
26	60.0	59.0	71.5	62.5	77	54	1	94	58	"
27	60.9	58.9	74.0	65.0	80	55	1	88	59	"
28	65.0	63.0	75.0	67.1	82	59	1	89	64	"
29	67.9	66.0	77.0	66.0	79	64	1	89	53	"
30	66.0	65.0	74.7	64.7	83	63	3	94	56	"
31	64.0	61.0	74.3	62.0	84	60	1	83	45	"

TABLE—*contd.*

Station—Alipore, Calcutta
Month and Year—January 1949

Date	At 8 hours I.S.T.		At 17 hours I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	RELATIVE HUMIDITY, PER CENT		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				At 8 hours I.S.T. °F.	At 17 hours I.S.T. °F.	
1	63.0	61.0	76.0	65.5	82	58	1	89	55	..
2	61.9	63.0	76.0	64.3	84	60	1	89	51	..
3	65.0	63.0	76.3	65.8	83	59	1	89	55	..
4	62.8	61.0	77.1	67.6	81	59	1	90	59	..
5	63.1	61.1	77.8	66.5	85	61	1	89	52	..
6	62.0	60.1	72.8	63.0	82	60	1	88	55	..
7	62.0	55.3	70.0	61.0	79	55	1	61	57	..
8	56.7	54.7	70.0	60.0	77	51	1	87	53	..
9	62.0	57.0	73.0	64.5	76	54	2	72	61	..
10	56.9	56.0	73.0	63.5	79	51	1	91	57	..
11	58.7	58.5	75.2	61.4	80	56	1	99	52	..
12	59.8	59.0	75.9	63.4	81	57	1	95	47	..
13	59.0	54.5	73.5	61.3	81	51	2	73	47	..
14	58.0	56.1	73.0	62.0	78	55	2	88	51	..
15	59.0	57.0	75.0	66.0	81	51	1	88	60	..
16	62.0	61.0	76.1	66.9	80	59	1	91	60	..
17	65.7	63.8	77.0	65.5	82	60	1	89	51	..
18	67.1	66.0	76.0	63.8	83	64	2	95	48	..
19	61.0	57.7	74.0	63.0	81	55	1	86	51	..
20	60.5	59.5	74.2	63.2	82	57	1	91	51	..
21	62.9	58.0	76.2	67.0	82	57	1	72	60	..
22	61.2	61.7	75.0	63.0	83	60	1	83	48	..
23	60.0	58.0	74.3	63.9	81	57	1	88	50	..
24	59.7	59.0	75.9	64.4	80	57	1	96	51	..
25	60.0	59.0	76.2	67.0	81	58	1	94	60	..
26	61.6	61.0	77.2	67.8	83	59	1	97	59	..
27	66.8	65.0	75.0	66.0	84	61	1	89	60	..
28	61.8	59.7	74.0	64.5	80	59	1	88	57	0.05
29	60.1	58.6	74.8	64.0	78	58	2	91	52	..
30	63.9	62.0	76.3	66.0	80	59	1	89	55	..
31	65.9	64.4	76.4	63.0	82	63	1	92	43	..

TABLE—*contd.*

Station—Alipore, Calcutta

Month and Year—December 1949

Date	At 8 HOURS I.S.T.		At 17 HOURS I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	RELATIVE HUMIDITY, PER CENT		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				At 8 hours I.S.T. °F.	At 17 hours I.S.T. °F.	
1	73.0	70.0	76.1	68.6	86	65	2	85	67	Nil
2	74.0	63.0	72.9	65.0	87	62	1	51	63	"
3	69.4	59.9	72.2	64.8	84	60	1	54	65	"
4	68.1	58.1	70.5	62.0	83	62	2	51	60	"
5	66.5	57.0	68.2	58.8	79	57	2	53	54	"
6	66.0	56.0	67.0	59.0	78	52	2	49	60	"
7	64.0	56.9	67.2	59.7	79	52	1	62	62	"
8	64.0	58.0	67.5	59.0	77	53	1	68	57	"
9	65.0	59.0	68.5	60.6	79	54	2	68	61	"
10	64.5	62.0	70.2	64.1	80	54	2	86	70	"
11	67.2	60.0	69.8	61.8	81	57	1	64	61	"
12	65.1	59.0	66.5	57.5	81	54	1	68	55	"
13	63.0	57.0	66.2	58.4	78	51	1	67	60	"
14	62.0	55.0	68.3	60.8	75	50	1	61	63	"
15	62.1	59.6	69.0	60.7	78	53	1	85	60	"
16	64.1	57.6	67.0	58.5	79	51	2	65	57	"
17	59.0	53.5	65.6	57.6	76	49	1	68	59	"
18	62.0	58.0	68.5	59.0	77	51	1	77	54	"
19	62.0	57.0	68.8	59.6	79	50	1	72	55	"
20	65.9	59.9	70.0	61.0	78	54	2	69	57	"
21	62.0	58.5	68.3	60.0	83	53	1	80	59	"
22	64.5	54.0	67.2	59.1	81	53	1	46	60	"
23	63.1	54.1	68.3	61.2	80	51	1	52	65	"
24	64.0	58.0	71.0	64.0	80	54	1	68	68	"
25	64.0	59.5	69.9	63.0	81	59	1	75	66	"
26	64.0	57.0	69.1	59.2	81	56	1	62	52	"
27	62.2	54.1	66.5	58.5	79	54	2	56	59	"
28	62.0	53.1	66.5	57.5	77	50	2	51	55	"
29	59.0	55.5	66.8	58.8	76	50	1	79	60	"
30	60.5	57.0	69.1	60.0	78	51	1	80	56	"
31	61.1	54.6	68.5	60.0	81	49	1	63	59	"

TABLE—concl'd.

Station—Alipore, Calcutta

Month and Year—January 1950

Date	At 8 HOURS I.S.T.		At 17 HOURS I.S.T.		Max.	Min.	Average wind velocity, M.P.H.	RELATIVE HUMIDITY, PER CENT		Rainfall in inches
	D.B., °F.	W.B., °F.	D.B., °F.	W.B., °F.				At 8 hours I.S.T. °F.	At 17 hours I.S.T. °F.	
1	62.7	60.2	71.5	62.0	80	53	1	86	55	Nil
2	64.2	63.9	73.2	62.1	83	59	1	98	51	"
3	66.5	59.5	72.1	63.0	86	59	2	64	58	"
4	64.8	56.3	70.3	62.3	83	59	2	56	61	"
5	59.5	52.5	67.4	56.4	79	53	2	59	46	"
6	62.0	54.5	69.2	52.1	76	52	2	59	65	"
7	62.1	56.6	70.3	61.8	77	55	2	69	59	"
8	62.0	57.1	69.5	60.8	78	55	2	72	58	"
9	63.0	55.0	68.5	58.5	79	52	2	57	52	"
10	62.0	53.0	65.6	55.2	78	53	2	51	47	"
11	59.0	51.0	66.1	56.9	73	47	2	54	54	"
12	57.9	54.0	68.7	58.9	75	48	1	76	53	"
13	60.9	54.5	70.0	61.0	79	50	1	63	57	"
14	64.0	57.0	71.0	62.5	80	53	1	62	60	"
15	65.0	62.5	71.2	63.1	80	57	1	86	62	"
16	66.0	63.1	75.0	67.0	81	58	1	84	64	"
17	73.3	66.2	78.0	69.0	84	65	4	67	61	"
18	67.0	62.8	74.3	63.8	86	60	4	78	53	"
19	64.0	61.8	77.0	67.1	84	59	1	88	57	"
20	68.2	64.1	76.0	66.0	86	62	1	79	57	"
21	69.1	64.1	77.0	68.0	85	63	1	75	61	"
22	71.0	63.0	76.7	66.2	85	64	1	62	55	"
23	70.0	62.8	76.1	64.1	86	61	1	65	49	"
24	64.4	59.5	75.3	63.3	85	57	1	73	48	"
25	67.7	59.0	75.0	65.0	85	57	1	56	56	"
26	65.7	65.0	75.1	65.2	85	60	1	96	56	"
27	68.0	61.0	78.0	68.1	84	61	1	65	58	"
28	69.1	63.1	75.8	62.3	84	63	2	70	43	"
29	67.5	61.0	76.1	63.9	82	59	2	67	49	"
30	68.0	62.0	77.3	65.3	83	58	1	70	49	"
31	69.5	69.0	80.0	69.1	85	65	2	97	55	"

air and that visibility was so poor that even natives of the area became lost.

'The first death during the smog had already occurred, however, early Saturday morning. . . . By 11.30 that night 17 persons were dead.

'On Sunday afternoon rain came to clear away the smog. But hundreds were still ill and the rest of the residents were still stunned by the number of deaths that had taken place during the preceding 36 hours'.

Such was the story of meteorological stasis over an industrialized area.

In 1930 a similar episode had occurred in the Meuse Valley of Belgium. Intense fog in a heavy industrial area had killed 60 persons.

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INDEX FOR VOLUME 84, 1949

THIS index which has been appended to the January 1950 issue may be detached and bound with the volume for 1949.

In connection with the numbering of the plates in volume 84, plates XXVII and XXVIII which follow plate XXIV may be corrected to plates XXV and XXVI respectively.

ERRATUM

The Vitamins, and Associated Substances and Considerations

In the above editorial, published in the October 1949 I.M.G., **84**, p. 454, line 21

for 'Vitamin B₁₂ is probably pteroyl-glutamic acid . . .'

read 'Vitamin B₁₂ is probably glutamic acid . . .'

Special Article

MAMMARY CARCINOMA

By P. N. RAY, M.B., F.R.C.S. (Eng.)
Calcutta

THE problem of cancer remains unsolved but the study of ever-increasing clinical material has opened up newer methods of investigation and treatment. In case of mammary carcinoma the vista has widened and new rays of hope are visible.

Incidence.—About 70 per cent of all cases occur in this country in Hindu women and about 20 per cent of them are nulliparous or childless widows. Incomplete evacuation of the lactating breast has been regarded as a contributing factor. This is unusual except in the upper and professional classes. In rural areas, it is not unusual for mothers to nurse their children for one or two years or even for a longer period. It is widely believed that prolonged lactation prevents pregnancy. In every 27 cases of cancer in women, 8 occur in the breast.

Age.—No age is immune but it is commonest around the fourth decade. It is fairly common in hospital practice to find a rapidly growing carcinoma during the period of lactation in the latter half of the third decade. Premenopausal malignancy is more virulent than the post-menopausal type.

Heredity.—Heredity is a factor which can no longer be regarded as a clinical coincidence. To mention one instance amongst many, breast cancer in the mother and a daughter or in two sisters has been noted. In another instance, two brothers died from carcinoma of the urinary tract and their unmarried sister died from carcinoma of the breast. Carcinoma in identical twins has been reported.

Milk factor.—The experimental study of breast cancer in mice has revealed the existence of a milk factor or virus-like body in the mother's milk. It is transmitted to the offspring through feeding. Obviously it is difficult to confirm its presence in human subjects.

Carcinogenic oestrogens.—All oestrogens are carcinogenic under certain conditions in experimental animals. Oestrogenic substances are naturally present in the adult ovary and are capable of inducing oestrus. Experimental production of carcinoma only occurs during the reproductive period of life. Paradoxical as it may seem, mammary carcinoma after menopause is marked arrest of progress and relief from oestrogens. Temporary

This effect is common of carcinoma of the breast on mamma

may be due either to the production of the mammatogenic hormone in the pituitary gland or to a direct action combined with that of the hormone of the pituitary gland. It is possible that lymphatic stasis and chronic inflammation are contributory factors. Chronic interstitial mastitis has long been regarded as a pre-cancerous condition.

Diagnosis

Diagnosis means early diagnosis. It is heart-breaking for the surgeon to see cases after cases of the so-called inoperable inoperable carcinoma.

Clinical examination.—In early cases, a small nodule or lump is noted, generally accidentally discovered by the patient during bath or when painful or tender during her monthly period. On inspection, the affected breast may appear to be smaller or elevated. Early deviation of the nipple when present is unmistakable. This results from involvement of the Cooper's suspensory ligament of the breast. The presence of a hard lump with ill-defined margins, elicited by the flat of the palpating hand against the chest wall of the patient, is almost pathognomonic. Such a lump if it does not disappear after the next monthly period with palliative treatment must be regarded as carcinoma until otherwise disproved.

The hyperplastic and cystic types of chronic mastitis are regarded as pre-cancerous conditions and would require careful watch. The left breast is more often the seat of malignancy and the commonest site is the upper and outer quadrant.

Transillumination.—The breast may be examined by transillumination with a suitable tubular light revealing the presence of cysts or solid lumps. This method should never be neglected.

Biopsy.—In early cases and in the pre-cancerous conditions, biopsy will be of invaluable help. The methods, generally employed, are aspiration biopsy, excisional biopsy and incisional biopsy.

(i) *Aspiration biopsy.*—Examination of the fluid will soon clear up the diagnosis of chronic cystic mastitis or a mammary cyst. The technique is simple but requires practice. A cutaneous wheal is first raised with local injection of novocain with a fine needle. A nick is made with a fine scalpel. Through this nick a painless aspiration will be carried out with an 18 gauge needle provided with a stylet, using a tight fitting record syringe. The droplet is spread out on a glass slide and a smear is then made. The report may be given by the pathologist within 15 minutes or so.

(ii) *Excisional biopsy.*—Complete excision of the lump with a broad margin with the diathermy knife is a commendable and a reliable method. When this is not practicable or desir-

able two parallel incisions are made with removal of the intervening skin. The incisions are carried through the breast down to the pectoral fascia.

(iii) *Incisional biopsy.*—By cutting directly into the tumour the risk of rapid dissemination is increased. The risk of local recurrence is also increased.

Clinical grouping

The commonest carcinoma of the breast is the scirrhus. The rapidly growing encephaloid or the acute inflammatory carcinoma is rightly regarded as unsuitable for mastectomy. The columnar-celled duct carcinoma characterized by a hæmorrhagic discharge from the nipple is probably the least malignant of these new growths. For purposes of surgical treatment, as elsewhere in the body, they are divided into three groups—

(1) Primary growth without any involvement of the area of lymphatic drainage.

(2) Primary growth with metastasis or enlarged lymph nodes. This group includes, fixity to the chest wall, peau d'orange, and a brawny arm due to lymphatic obstruction.

(3) Inoperable and inoperable carcinoma.

The prognosis is best in the first case but even then it will depend on the size, situation and character of the new growth. The second group comprises the majority of cases. The rates of operability and recurrence will vary within wide limits. The third group comprising ulcerating, fungating and foul-smelling growths are still too familiar to need any commentary. The large sized benign cystadenoma, when ulcerated, may be mistaken for a carcinoma. Owing to secondary infection, it may become fixed to the chest wall and axillary glands may become enlarged and matted. In such cases incisional biopsy is helpful. In one case mammary actinomycosis was differentiated with difficulty.

Treatment

It is important to remember that in every case of malignant disease the treatment is two-fold—(a) treatment of the primary growth and (b) treatment of the area of lymphatic drainage or metastasis. The controversy regarding merits of radical mastectomy and irradiation therapy is no longer irreconcilable. Experience has led to a judicious combination of the two methods.

(1) In this group, radical mastectomy with immediate implantation of radium needles is probably the method of choice. A carefully calculated dosage of radium in the form of 2 mg. needles is spread out giving special attention to the axillary and mediastinal lymph nodes.

(2) The same procedure may be adopted. But opinion is equally divided on a post-operative deep x-ray therapy.

(3) Only palliative treatment is possible in this group of advanced cases. If the neoplasm has not ulcerated, irradiation treatment with implantation of radium needles is to be preferred. Local excision of the growth, whenever possible, is carried out. But metastatic lymphatic glands in the axilla and the mediastinum will require heavy doses of deep x-ray. Deep x-ray therapy is not without danger, it therefore must be undertaken by skilled and experienced radiologists. Lymphatic oedema of the arm is an unpleasant sequela; Kondoleon's operation has been tried but the result is generally unsatisfactory.

Prognosis.—Great divergence of surgical opinion still prevails. In group (1) the 5 years' survival rate is calculated as 65 to 90 per cent. In group (2) this rate is not expected to exceed 50 per cent. Much depends on the size, site and pathological characters of the new growth.

Hormonal treatment.—In group (3) cases or after post-operative recurrence, androgenic hormone therapy with testosterone propionate up to 250 mg. daily or stilboestrol and allied synthetic oestrogens may give remarkable results with temporary regression of progress and relief of pain particularly in post-menopausal cases.

Conclusion.—Early diagnosis and radical mastectomy combined with immediate radium irradiation or post-operative deep x-ray therapy is the procedure of choice ensuring 5 years' survival. In other cases with involvement of skin, chest wall and lymph nodes, a 5-year survival period is not to be expected. But in certain post-menopausal cases beneficial results have been obtained after treatment with androgenic hormones and paradoxically as it may appear with certain synthetic oestrogens. It has opened up a new line of study and treatment of mammary carcinoma.

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Medical News

SCIENCE IN AID OF HUMAN WELFARE. FIRST NATIONAL LABORATORY TO BE OPENED. A VISION REALIZED

(From a Release issued by Press Information Bureau, Government of India, dated 3rd January, 1950)

WITH the opening of the National Chemical Laboratory by the Prime Minister, Pandit Nehru, to-day at Poona, an important landmark in the establishment of

scientific research on a planned basis in India will have been taken. The Laboratory which is the first of the eleven national laboratories proposed to be established by the Government of India all over the country aims at application of research to the needs of the industry with a view to augmenting the resources of human welfare.

Indian industry, if it is to develop sufficiently well to stand in comparison with the progress made by advanced Western countries, needs not only a substantial improvement in the quality of its output but also new products have to be evolved out of the large resources of raw materials available in the country.

Science and Indian Welfare

Scientific knowledge in India is of no mean order: individually, Indian scientists have received world-wide recognition for their scientific attainments, but till recently, progress in the industrial fields has not been in keeping with the country's needs and demands. One of the main functions of the National Chemical Laboratory will be to bridge the gulf between the scientific research and its application to problems of human welfare. It will take up long-range problems of fundamental research in chemistry and also problems not usually tackled in universities for lack of funds or for lack of facilities.

Located on a 470-acre site in Poona, the building is 600 feet long, 200 feet wide and has over 150 rooms, including an auditorium, library, seminar and sectional laboratories. Some of the rooms have been specially equipped for applied research.

Link with Industry

The Laboratory will also provide a link between the universities and research institutions on the one hand and Indian industries on the other. The need for such an organization for development of the industry has been recognized in all advanced countries and well-equipped laboratories exist which deal with problems of such a nature. In Western countries, technical processes have been developed which have revolutionized industrial development, and in fact, modern civilization itself. Such work naturally requires concentration of effort at the highest scientific level and also, incidentally, expenditure. But the effort has been worth while making. For example, utilization of coal tar, fixation of atmospheric nitrogen, development of plastic and artificial rubber, artificial textiles and fabrics, hydrogenation of coal and development of the petroleum industry are only a few of the important discoveries which would indicate what science can do for the progress of mankind. The National Chemical Laboratory hopes to undertake such difficult but important items of research. Its services will cover such a wide range of subjects as cosmetics and perfumes, vitamins, gas products, industrial gases, etc.

To ensure co-ordinated endeavour to cover all aspects of research, the Chemical Laboratory, although so named because its main function will be chemistry, will embrace other allied sciences like physics, mineralogy, engineering and biology in so far as they relate to chemical problems and the chemical utilization of national resources. Without such co-ordination, the Laboratory may become sterile.

The Laboratory will also provide training of research workers in specialized fields of chemistry and technology, particularly on those aspects of research for which no provision exists in scientific laboratories in the country.

Work already done

Although the Laboratory is being formally opened to-day, it has been functioning in some form ever since its inception in 1940 when the Board of Scientific and Industrial Research with Dr. S. S. Bhatnagar as the Director was formed. A measure necessitated by the emergency of the war, this Board was required to

utilize and co-ordinate the work of existing organizations, to survey the work that was being done by them, to invite proposals from all sources, to initiate discussions and to make recommendations to the Government of India on the general lines on which industrial research should be undertaken and pursued. On the basis of the work carried out in the laboratories, 150 patents have been taken and nearly 120 scientific papers have been published.

Professor McBain

The first Director of the Laboratory is Professor James W. McBain, F.R.S., who is a recognized authority on physical chemistry and has done considerable scientific work during the two World Wars. He has published as many as 400 scientific papers on various topics in the fields of physical chemistry. Before joining the present post, Dr. McBain was Professor of Chemistry Emeritus at Stanford University of California.

PLAGUE

By GEORGES BLANC

Director of the Pasteur Institute of Morocco

(From Special Feature No. 4, dated November 1949, issued by W.H.O. Public Information Office, Geneva)

THE history of plague is a long and dark one. Even to-day the name itself, with its association of swift and widespread death, brings terror to the people of many lands. So sudden were its visitations in Europe that Ambroise Paré, a famous French physician of the sixteenth century, called the malady 'tempestuous'.

Coming out of Asia, plague first invaded Europe, via Byzantium, in the sixth century, during the reign of the Emperor Justinian. It was then that Procopius, the Byzantine historian, gave a precise description of the effect of plague on the human body, observing that it brought about blood-poisoning and inflammation of the lymphatic glands.

After several successive waves of plague had spread over Europe, the disease appeared to lie low for nearly three hundred years. Then, in the fourteenth century, the terror revived. This was the time of the 'Black Death' which devastated Europe, wiping out over a third of the total population. Time and again the terror struck, the attacks continuing until the eighteenth century. When in 1720 it re-entered Marseilles to claim 40,000 victims, it had already left hundreds of thousands dead in its path, including 70,000 in the London of 1665.

Crude Defence in Middle Ages

The panic created by the mysterious disease led to the adoption of crude methods of defence. Infected houses were fumigated and marked with a cross, and no one was allowed to enter. Doctors wore cowls, and their clothes also bore the sign of the cross. People stepped back at their approach with apprehension, or even with hostility.

It was forbidden for anyone from an infected zone to enter a healthy city. Those caught attempting to do so were turned back after having their ears cropped. The sight of persons whose ears had been cut off was not uncommon.

The rapid and unpredictable movement of the 'Black Death' gave rise to rumours that it was being deliberately spread. The accusation was made that fat from corpses was being smeared on the doors of houses. Many unfortunates were declared to be guilty of this offence and put to death.

Plague was believed to be a manifestation of divine wrath and the saints were called on to intercede on

behalf of mankind, the most celebrated being St. Roch, popular pictures of whom are still to be seen showing him with the thigh gland enlarged—a symptom of the disease—and at his feet the dog that had saved him from starvation when he was cast out as plague-stricken.

The many parishes of St. Roch to-day bear witness to the fact that plague had visited them, and so caused them to adopt the saint's name in the hope of obtaining his personal intercession.

The realization that plague was spread through contagion developed with increasing force, and in the fifteenth century the Venetians set up the first isolation ward and created quarantine.

Eradication Foreseen To-day

Although plague left Europe in the eighteenth century, it has remained in the Orient where its ravages still continue. 100,000 died of it in Canton in 1894. In the same year it reached Hong Kong, where Yersin discovered the bacillus that now bears his name. In 1896, Roux and Yersin showed that the bacillus was identical with that found in infected rats. Finally, in 1898, Simond demonstrated that the disease is carried by the rat flea.

With a few further years all the relevant facts about the disease were co-ordinated, and shortly after was added knowledge of the type of infection carried by wild rodents, now known as sylvatic plague. By now the fight against the 'Black Death' had commenced along planned lines by means of destruction of rats, isolation of individuals in contact with infected persons, quarantine, and the use of treatment sera and preventive vaccines.

In recent years great progress has been made. The discovery of powerful insecticides such as DDT, and of efficient therapeutics such as the sulpha drugs and streptomycin have given greater hope for conquering this age-old scourge. The World Health Organization has formed an Expert Committee on Plague for the purpose of combining all known methods of attack against what was once an almost unknown enemy. During the recent meeting of this Committee, held at W.H.O. Headquarters in Geneva, a system was planned for the compilation and assessment of all existing data, the carrying out of full treatment measures and the detailing of methods of eradication of plague centres.

It is planned that a group of specialists in the field will be sent to India, where the disease to-day presents a very grave problem. There they will demonstrate plague eradication work for the first time on an international scale. Other demonstration areas for plague eradication recommended by the W.H.O. Expert Committee include one of the infected islands off the coast of Africa (Azores or Madagascar), Morocco, the Belgian Congo, and China.

In these plague centres the use of DDT, '1080' (sodium fluoroacetate), and streptomycin, combined with the expert knowledge available to-day, will demonstrate in actual practice the ability of modern science to conquer one of man's most dreaded enemies.

9TH BENGAL PROVINCIAL MEDICAL CONFERENCE

PRESIDING over the Conference held in December, Dr. Amulyadhan Mukharji said that there are about 12 thousand qualified doctors in West Bengal for a population of 2 crores and a half. In 93 towns, about 90 lakhs of people and in 34,249 villages, about one crore and 60 thousand people live. The ratio of doctors to population comes out at one doctor for about 2,000 people in West Bengal. This is not so bad as people generally assert. Due to absolute lack of communications in rural areas, most of the villages are not

accessible by vehicles during rainy season, villages even at a distance of 8 or 10 miles from Calcutta cannot be reached. Thus even if qualified medical men trained in scientific methods are stationed nearby, their services can hardly be utilized by the people at large. Although the nation is supposed to live in the villages where diseases are much more rampant and where food and raw materials are produced, people are neglected very badly. Unless communications are improved, water supply is bettered, education is extended and the economic prosperity of the people is raised, mere production of a large number of qualified doctors will not solve the problem.

Dr. Mukharji said that appointments should be made by open competition held by Public Service Commission from amongst all registered medical practitioners and merit and experience should be the only criteria for recruitment. Medical men with high technical qualifications should be appointed in the teaching line and periodically they should be sent abroad, not to acquire degrees and diplomas, but to acquaint themselves with improved techniques.

The Rural Health Scheme, adopted by the Government of West Bengal which envisages the creation gradually of 2,053 rural and 272 thana centres, could not develop as per anticipations of all. Up to date, only 2 thana and 16 rural health centres have started functioning and some 25 more may start this year. This also is likely to be handicapped due to the financial conditions of the central and provincial governments. To improve medical relief, more funds are needed. People resent the imposition of direct taxes. Dr. Mukharji suggested that for the present half the number of beds in all public hospitals should be paying and in outdoor also people of better means will have to be charged and, with the money thus available, the indigent and poor can be served free. The scheme of having only one doctor for each rural centre, on Rs. 150 only per month without the right of private practice, should be revised. The Thana Health Centre Scheme now in operation should be thoroughly re-cast and the dual control of District Board and Government should cease. He suggested that every medical student should stay at least for three months in rural areas to see conditions there and adapt himself to them. He condemned the honorary system in all public hospitals and allotments of large number of beds to individuals.

He cautioned the medical men to be careful to safeguard their interests as advocates of modern scientific medicine, as attempts for definite inroads into their spheres by homœopaths, kavirajes, and quacks are on the way and a section of the public is seen to lend its support to these charlatans. He expressed his concern at the display of sympathy of those in power towards the Ayurveda and Homœopathic systems which are not based on research and science and the move to synthesize which with the modern scientific system will introduce complications of a far-reaching character. He also urged indigenous manufacturers to stick to standard and asked the profession to prescribe these products if they are based on quality.

DRUGS RULES, 1945

Amendments to Schedule K and Forms 20 and 21 to Schedule A

No. F.1-56/47-D, Government of India, Ministry of Health, New Delhi, the 16th January, 1950

NOTIFICATION

IN exercise of the powers conferred by section 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said section, namely:—

In the Schedules annexed to the said rules:—

I. In Schedule A—

(1) For the heading of Form 20, the following heading shall be substituted, namely:—

'Licence to sell, stock and exhibit for sale and distribute drugs other than biological and special products specified in Schedule C'

(2) In the heading of Form 21, the word 'Other' shall be omitted.

II. In Schedule K, item 2 shall be omitted.

(Sd.) J. N. SAKSENA,
Under Secretary.

'SABHARWAL',

16th January, 1950.

ASSOCIATION OF PHYSICIANS OF INDIA

The Annual Conference of the Association of Physicians of India will be held at Lucknow on the 15th, 16th and 17th March, 1950.*

There will be symposia on:—

(1) Ankylostomiasis.

(2) Peptic ulcer.

(3) Treatment of malaria.

There will also be papers on other subjects read at the Conference.

All physicians and those interested in the above subjects are invited to contribute papers and take part in the discussions and in the Conference.

Those wishing to attend the session should write to Dr. S. S. Misra, 12, Clyde Road, Lucknow, for accommodation.

THE 16TH ANDHRA PROVINCIAL MEDICAL CONFERENCE

(INDIAN MEDICAL ASSOCIATION)

The Conference will be held in Bezwada on 7th and 8th April, 1950. There will be an interesting scientific exhibition, medical film shows, as well as of pharmaceutical products, surgical implements, etc.

Lodging and boarding facilities are provided for delegates at Rs. 5 per day and they are requested to intimate the Secretary in advance.

Members desirous of reading scientific papers are requested to send a copy of the paper to the Secretary, at least 15 days before the Conference.

All further information can be had from Dr. N. L. Sastry, Secretary, Reception Committee, Andhra Provincial Medical Conference, Bezwada.

INDIAN SCIENTIST ACCEPTS HIGH POST IN W.H.O.

(Reproduced from Press Release SEA/PR/50-12, dated 2nd March, 1950, issued by World Health Organization, Regional Office for S.E. Asia)

MAJOR-GENERAL SIR SAHIB SINGH SOKHEY, who for the last 18 years has directed the Haflkine Institute, Bombay, has now accepted a high international post as Assistant Director-General of the World Health Organization, it was announced this morning. Very shortly he is to leave India to take up his new duties in Geneva, Switzerland.

Dr. Sokhey's work is known and respected by scientists and medical men throughout the world. He

* Received late for publication.—Editor, I.M.G.

is an outstanding authority on plague and cholera. Under his leadership important progress has been made in the production of plague and cholera vaccine and anti-snake venom serum, while the present reputation of the Haffkine Institute as one of the famous laboratories of the world may be said to be due almost entirely to his energy and initiative.

At the same time, Dr. Sokhey has devoted much attention to field work, and he has played an important part in recent advances in methods of treating plague in particular.

In medical circles, considerable satisfaction is felt that Dr. Sokhey, who has now reached the age of retirement from the Haffkine Institute, has the opportunity to continue his labours in an even wider sphere.

At Geneva Headquarters of W.H.O., Dr. Sokhey will succeed Dr. Raymond Gautier as Assistant Director-General in charge of the Department of Technical Services which includes the Divisions of Epidemiology, Health Statistics and Therapeutic Substances. The Department of Advisory Services, responsible for field work and direct assistance to Governments, is under another Assistant Director-General, Dr. Martha Eliot (U.S.A.), who visited India last September.

The Director-General of W.H.O. is Dr. Brock Chisholm of Canada.

MEETING MEDICAL PROFESSION'S NEED OF DRUGS AND SURGICAL INSTRUMENTS: MORE LIBERAL IMPORT POLICY

(Reproduced from a Release dated 23rd January, 1950, issued by Press Information Bureau, Government of India)

WHILE industries for the manufacture of the medical profession's requirements are being built up in India, it is clear that for some time this country will have to import, within her limited foreign exchange resources, many hospital drugs and medicines, such as insulin, penicillin, streptomycin and sulpha products, which are integral to modern curative technique, together with up-to-date surgical instruments and appliances.

In accordance with this policy, the importation of essential drugs from soft currency areas was under Open General Licence up to 15th September, 1949. Subsequently, a watch was kept on stocks in the country and during the last half-yearly shipping period ample provision was made by the Import Control authorities for the intake of essential drugs from hard and soft currency areas. These included insulin, penicillin, streptomycin and other essential drugs, such as vitamins and sulpha drugs. More recently, the position has been reviewed and now these drugs, including some like streptomycin obtainable only from hard currency areas, are being licensed for import in good quantity.

Reliable reports from the chemists and druggists are that with the possible exception of penicillin, ample supplies of drugs are available in the market. In the case of penicillin, it is now understood that accredited agents in India of leading American firms have received licences for the import of procaine penicillin for sale to Indian buyers, and supplies should be on their way to this country. Similarly, supplies of penicillin G from the United Kingdom should be arriving shortly. Licences for the import of considerable quantities of streptomycin from dollar areas have also been recently issued by the Chief Controller of Imports.

SURGEONS' REQUIREMENTS

Regarding the need for surgical instruments and appliances, these items were under Open General Licence up to 31st May, 1949. Thereafter, a measure of control was applied, but certain licences continued to be issued under the OGL concession scheme. Immediate steps

are being taken to liberalize import policy in such a manner as to cover the whole range of surgical instruments and appliances.

At present small quantities of general surgical instruments and appliances are available from firms in Calcutta and Bombay, but besides very limited production capacities, the quality of the products does not always maintain accepted standards. A Board has been formed with the Director-General, Industry and Supply, as its head to examine the possibilities of aiding manufacturers from Sialkot now in India in establishing firms in this country. It is obvious, however, that until the supply position improves considerably, imports of surgical instruments and appliances, some of which are of daily use in hospitals and clinics, will have to continue, and arrangements are being made to procure these supplies from the U.K.

W.H.O. EXECUTIVE MEETS IN GENEVA

(Reproduced from Press Release SEA/PR/50-3, dated New Delhi, 16th January, 1950, issued by World Health Organization, Regional Office for S.-E. Asia)

DR. C. MANI, Regional Director for South-East Asia Regional Office of W.H.O., arrived in Geneva on Sunday, 15th January, to attend the meeting of the 5th session of the W.H.O. Executive Board, which opens on Monday the 16th. The sessions are under the Chairmanship of Sir Arcot Lakshmanaswamy Mudaliar, Vice-Chancellor of the Madras University, and will last until the second day of February.

Two important items are on the agenda to be reported upon by a six-man standing committee on administration and finance. This committee has been meeting at W.H.O. Headquarters in Geneva for the past ten days. One of the important items is on organizational structure and administrative efficiency in the carrying out of W.H.O.'s public health programme throughout the world. The second important matter to be reported upon pertains to the proposed 1951 programme and budget for the organization.

The W.H.O. Executive Board will also consider recommendations made by the three Regional Organizations now in operation. These three regions are the South-East Asia Region with Headquarters in New Delhi, the Eastern Mediterranean Region with Headquarters in Alexandria, Egypt, and the Americas Region with Headquarters in Washington, D.C. In addition, the agenda of the W.H.O. Executive Board will include constitutional problems and amendments to the W.H.O. Constitution proposed by Australia, Denmark, India, Norway and Sweden. The Executive Board is composed of the following members designated by their respective governments and representing the Health Assembly of W.H.O. as a whole:

Dr. de Paula Souza, Director and Professor, Faculty of Hygiene and Public Health, University of Sao Paulo.

Prof. J. Parisot, Professor d'Hygiene et de Medecine Sociale a la Faculte de Medecine de Nancy.

Dr. M. Nazif Bey, Assistant Under-Secretary of State, Ministry of Public Health, Cairo.

Sir A. L. Mudaliar, Vice-Chancellor of Madras University.

Prof. M. De Laet, Secrétaire General du Ministère de la Santé publique et de la Famille, Bruxelles.

Dr. V. J. Babecki, Inspector, Ministry of Health, Warsaw.

Dr. Melville Mackenzie, Principal Medical Officer, Ministry of Health, London.

Dr. H. Hyde, Medical Director, U.S. Public Health Service, Federal Security Agency, Washington, D.C.

Dr. A. Stamper, President of the Yugoslav Academy of Sciences and Arts; Professor of Public Health and Social Medicine, University of Zagreb.

Dr. H. S. Gear, Deputy Chief Health Officer for the Union of South Africa.

Dr. A. Villirama, Secretary (Minister) of Health, Manila.

Dr. J. A. Hojer, Director-General of Public Health, Stockholm.

Dr. E. Tok, Under-Secretary of State, Ministry of Health and Social Assistance, Ankara.

Dr. E. Tejera, former Minister of Health and Social Welfare, Professeur de Pathologie tropicale, Caracas.

W.H.O. EXPERTS ON DRUG ADDICTION MEET TO ADVISE U.N.

(Reproduced from Press Release SEA/PR/50-2, dated New Delhi, 16th January, 1950, issued by World Health Organization, Regional Office for S.-E. Asia)

THE meeting of the W.H.O. Expert Committee on Habit-Forming Drugs which began in Geneva on 9th January to advise the United Nations on various problems connected with drug addictions, and more especially with international control of new synthetic substances, is expected to make its final recommendations this week.

The Committee includes Dr. N. B. Eddy, of Washington (Chairman), Dr. J. Bouquet, of Tunis and Dr. J. R. Nicholls, of London. In addition, three consultants are participating in the meeting. They are Professor Rogelio E. Carratala, of Buenos Aires, Professor Sir Ram Nath Chopra, of Srinagar, Kashmir, and Professor Georgios Joachimoglu, of Athens.

Authority for the World Health Organization to participate in international control of narcotics derives from three diplomatic instruments, the Second Opium Conference (Geneva, 1925), the 1931 Convention (for limiting the Manufacture and Regulating the Distribution of Narcotic Drugs), and the 1948 Paris Protocol, bringing under international control drugs outside the scope of the 1931 Convention.

The findings of the Committee, in so far as the drugs coming under the 1925 Conference are concerned, can be only recommendations. Their application depends on the consent of the contracting party concerned. But the decisions taken by the World Health Organization according to the 1931 Convention and the Paris Protocol, which entered into force on 1st December, 1949, are immediately binding on all parties to these instruments. In the exercise of its functions, the World Health Organization acts as a treaty organ on behalf of the 71 States which are party to one or more conventions. The Paris Protocol covers the new synthetic drugs capable of producing addiction or convertible into such. Their number is constantly increasing. At its first session, held in January 1949, the W.H.O. Expert Committee took steps to bring under international control a whole group of synthetic substances of the *Pethidine* and *Methadone* type.

The agenda of the present session includes consideration of the resolutions taken by the Economic and Social Council on 6th July, 1949, asking governments to put into effect the W.H.O. recommendations as to the control of synthetic drugs of the *Pethidine* and *Methadone* type, and various requests of the Council and of the Narcotics Commission. The experts will further examine the situation as regards morphine derivatives, diacetylmorphine (heroin, diamorphine) and synthetic substances. Problems referred to this Committee by the W.H.O. experts on mental health and on the unification of pharmacopœias will be considered during the meetings.

ACCIDENT PREVENTION IN FACTORIES. HOW BRITAIN SAFEGUARDS WORKERS' HEALTH

By S. GORDON COLLIER

(From Release No. B.F. 53, issued by the British Information Services, New Delhi)

IN the continuous process of mechanizing and modernizing production methods in industry, new risks to the safety and health of workers are constantly arising. The production drive which is now in full swing in Britain has, therefore, brought fresh problems to the Factory Department of the Ministry of Labour in London, which is using all the latest weapons of scientific research to fight these new dangers. Some of the results of this battle have just been described in the annual report of the Chief Inspector of Factories for 1948.

Though there was a slight increase in the number of fatal accidents as compared with 1947, the report records a steady decrease, year by year, in the total number of notifiable accidents in British factories since 1944, when the figure was 266,766. Taking this figure as 100, the number of accidents in 1945 was reduced to 85 per cent, in 1946 to 78 per cent, in 1947 to 70 per cent, and in 1948—the year covered in the report—to 69 per cent (the total number of accidents was 182,838).

This result does not, however, allow for changes in the number of persons employed, a more accurate measure of the progress being the accident rate, that is the number of notifiable accidents per 1,000 employees. This figure fell in the same period from 40 to 28, a reduction of 30 per cent.

FREQUENCY RATE

Even more accurate is the Frequency Rate, which gives the number of accidents causing loss of time beyond one day or shift for every 100,000 man-hours worked. In Britain, this figure in 1948 was only 2.19 for a sample of 1,158 factories employing nearly one-fifth of all workers in British industry, compared with 2.27 in the previous year for a slightly smaller sample. For 28 factories in which records have been kept regularly since 1944, the rate has fallen every year without exception from 2.52 in the first year to 1.88 in 1948.

The conquest of industrial diseases is also progressing apace, as is seen clearly when a comparison is made with the figures for the beginning of this century. Cases of lead poisoning, for instance, which totalled 1,058 in 1900 (with 38 deaths) were down to 49 (with two deaths) in 1948. The year under review was also only the second since 1899 when no fatal case of anthrax was reported, the 32 cases known in 1948 having been successfully treated with penicillin and a British-made serum distributed to public health laboratories throughout the country.

Turning to the new problems introduced by the production drive, the report states that 'radiological hazards in industry form a subject of rapidly growing importance'. It instances the use of radio-active materials to disperse static electricity in the printing and textile trades.

One large printing firm, which had had trouble for years in printing cellophane wrappings because static electricity caused the wrappers to 'balloon' as they went through the machine, had fixed flat bars across the machines faced with thin gold or platinum foils containing a radium salt in solid solution. The alpha, beta and gamma rays from the salt dissipate the static charges, while the care taken to direct the radiations away from the workers has made the dangers very small.

RADIO-ACTIVE DUST

The microscopic examination of dust has been widely used to fight this insidious enemy of workers' health. A serious case of disease in the shredding department of a factory handling bagasse led to photo-micrographs

of dust samples and a new hydraulic vortex method of opening and breaking up the bales under water. In an atomic energy factory, the fine dust which was entering the plant from outside and becoming radioactive as a result was examined in the same way, and the air filtration system was consequently re-designed.

The report quotes many instances where the introduction of mechanical handling and new equipment has brought not only more efficient output but also fewer dangers to the safety of workers. In the rubber industry, the use of conveyors which feed material automatically from one machine to the next has cut out dangerous hand-feeding. In the vulcanizing of rubber tyres for motor-cars, where formerly the moulds had to be manipulated by dangerous lifting tackle, the worker now handles only the tyres or tubes, feeds the work to the machines, and presses a button.

In a paper mill, where the paper has to be fed into high-speed calender rollers, a chute with air jets has kept the operator away from this danger point. Accidents due to the collapse of foundation trenches for buildings have been tackled by a machine which makes deep trenches unnecessary, since it bores holes in which concrete piles are cast to support a footing beam for the wall.

TOWARDS HIGHER OUTPUT

New equipment for blast furnaces in the iron and steel industry has kept the temperature in totally enclosed cast houses down to five degrees above the outside temperature. Dust in cardrooms at cotton mills has been halved by oiling the cotton with a new substance, higher output and easier spinning being other results of the new process.

The report also describes developments in joint consultation, and the increasing provision for the welfare of workers, including a rise in the number of factories providing hot meal canteens from 13,235 to 14,717 during 1948. Cheerful colour schemes in factories have helped towards higher output.

DELHI TO HOUSE ONE OF ASIA'S LARGEST, AND MOST MODERN SCIENTIFIC INSTITUTIONS

OPENING OF NATIONAL PHYSICAL LABORATORY ON
21ST JANUARY

(From a Release dated New Delhi, 13th January, 1950, issued by Press Information Bureau, Government of India)

JANUARY 1950 will be remembered for two major events in the field of scientific development calculated to be of invaluable benefit to India's industrial progress. The Hon'ble Sardar Vallabhbhai Patel, Deputy Prime Minister, is to open the National Physical Laboratory at Hillside Road, New Delhi, on 21st January—less than three weeks after the Prime Minister inaugurated the National Chemical Laboratory at Poona.

Scientific research on a planned national basis was visualized first by Dr. S. S. Bhatnagar, F.R.S., Director of Scientific and Industrial Research, whose proposals to establish five national laboratories under the aegis of the Council of Scientific and Industrial Research received the Government of India's approval in 1944, a grant of Rs. one crore being set apart for this purpose, as a post-war measure. It was not long before the scheme aroused the interest of organized industry, and several valuable donations in cash and kind were made to the Council.

Under Dr. Bhatnagar's direction, the work of planning was immediately taken in hand and by 1946 details of all five laboratories had been drawn up and grants earmarked.

PRIME MINISTER'S INTEREST

With the advent of the National Government, and the keen interest displayed by the Prime Minister in scientific research, expenditure for the establishment of six more national laboratories was sanctioned. Thus, a chain of no less than 11 national laboratories in various parts of India was envisaged and construction in some cases began in 1947.

It was in that year that Pandit Jawaharlal Nehru laid the foundation stone of the National Physical Laboratory, and with its opening two years later, India becomes the proud possessor of one of the largest institutions of this kind in Asia besides one of the most modern in the Commonwealth.

RESEARCH ON FUNDAMENTAL STANDARDS

Housed in an imposing building and an area towards which the Metropolis is extending its tentacles, the Physical Laboratory will undertake, as its main function, research on fundamental standards of length, mass and time and their derived standards. It will work through the following divisions: Weights and Measures, Applied Mechanics and Materials, Heat and Power, Optics, Electricity, Electronics and Sound, Applied Physics, Hydraulic Research and Analytical Chemistry.

Research will also be undertaken on fundamental and applied aspects, and the laboratory will endeavour to assist in the fullest utilization of India's raw materials and natural facilities, to improve and standardize methods and processes and increase industrial efficiency so as to reduce costs of production.

At present, India has no precise physical measurements, such as length, mass and time, which could claim statutory acceptance or be duplicated with scientific exactness for the benefit of industry. There is hardly an agency in the country which could act as a referee in the matter of industrial standards, nor any laboratory where research work required for the formulation or revision of specifications could be undertaken. The Physical Laboratory is designed to supply this want.

WORK ALREADY IN PROGRESS

Work on important aspects of applied physics and fundamental physics has not awaited the Laboratory's formal opening. Dr. K. S. Krishnan, F.R.S., Director of the National Physical Laboratory, who has a large volume of scientific work to his credit, has been able since its opening to contribute to the structure of crystals and the behaviour of plastic materials. The scope of these activities is expected to be enlarged considerably with the use of additional facilities and equipment which the Laboratory will provide.

Specialized equipment and precision instruments have been secured from abroad and also as a result of careful selection and scrutiny among the various disposal organizations of the Government of India. This equipment should assist the Laboratory to go into full operation with the least possible delay, once electricity, water, gas and other services have been provided.

10,000-BOOK LIBRARY

Besides its valuable apparatus for precision work, the Laboratory will have one of the best equipped libraries on physical science. Nearly 10,000 books have been obtained and more are on order. Also, 250 or so scientific journals are being received.

A large and well-equipped workshop, a gas house and a cafeteria will be additional features of the Laboratory, which will also accommodate the laboratories of the Defence Science Organization now housed in Delhi University. The Laboratory's unique facilities and services may also be made available to other departments of the Government for their work.

Public Health Section

PROTECTIVE VALUE OF BCG
VACCINATION

REVIEW AND DIGEST OF MAJOR PUBLICATIONS

(Issued by the International Tuberculosis Campaign)

ALTHOUGH BCG vaccination has been brought to the attention of the public a number of times in the course of the last thirty years, only relatively few persons besides the specialists interested in the prevention and control of tuberculosis are fully aware of the developments in this field of medicine.

The very character of the tuberculous infection, its chronic nature as a disease, the distribution in an endemic form all over the world are such that true evidence of the efficacy of the vaccine can be obtained only by statistical studies. A reliable study of this kind should not only provide for a follow-up of many years of the material under observation but also for a control group of non-vaccinated persons exactly comparable with the group of those vaccinated. It is evident that such experiments, involving hundreds if not thousands of persons to be controlled during a long period of time, are extremely difficult to carry out. Nevertheless, several studies of this kind have been attempted and the results have justified the use of the vaccine in the fight against tuberculosis throughout the world. Much work has also been done both in laboratories and on animals to improve efficiency and innocuity of the vaccine as well as techniques and indications for vaccination.

The vaccine was used on human beings for the first time by Weill Halle (1925) in 1921 when he administered it orally to a newborn child, after Calmette and Guérin had studied the properties of BCG, the *Bacillus Calmette Guérin* as it was called, for more than ten years *in vitro* and on animals. Soon mass vaccination of children by the oral method, as advocated by Calmette (1928), was carried out on a fairly large scale in several countries. By the end of 1928, more than 116,000 children had received BCG in France alone. This method, however, lost much of its prestige when it appeared that there were no substantial clinical nor statistical proofs of the efficiency and harmlessness of the vaccine [Wallgren (1927), Greenwood (1928), Rosenfeld (1928), etc.]. The fact that only 5 to 30 per cent of the children became sensitive to tuberculin after receiving BCG orally reduced markedly the epidemiological value of the vaccination. Furthermore, the Lübeck tragedy, although not caused by BCG, as was definitely established by a German court (1935), made oral vaccination unpopular. The court on the basis of bacteriological examinations, determined that vials of virulent tubercle bacilli of a known strain used for laboratory experiments were accidentally substituted for vials of BCG. To-day the oral method is still used in some countries, mainly for the immunization of newborns in tuberculous families, as in Roumania and in Poland, or on a larger scale as in Brazil (1947).

Parenteral administration of the vaccine was begun around 1927 in Scandinavia; Heimbeck in Norway injected it subcutaneously, Wallgren in Sweden used it intradermally. The latter method has now been very widely adopted although other techniques are also being used to some extent; Rosenthal's multipuncture (1939), scarification by the method of Negre and Bretey (1947).

Wallgren (1934), a pediatrician, was the first to show the importance of BCG in the control of tuberculosis in a community injecting all the children of tuberculous families and those exposed to infectious sources in the town of Gothenburg, in Sweden, and he obtained a sudden drop in the mortality rates from tuberculosis in the younger age groups. Whenever possible, the children

were isolated from the source of infection for six weeks before vaccination and afterwards until allergy had developed. Thus a total of 1,069 persons were given BCG intradermally in the period 1927-1937 in Gothenburg alone. Anderson and Belfrage (1939), in 1939, made a study of this material and were able to re-examine 905 vaccinated persons. They found that tuberculous disease had developed in two cases only, and in a benign form. Furthermore, a small child had died from a specific primary infection, with generalization which had developed three weeks after vaccination. This child had not been isolated prior to the vaccination and it must be presumed that BCG had been inoculated in the incubation period.

Observations made by Heimbeck (1948) in the years 1924-1926 on probationers entering the nursing school of the Ullevaal Hospital on Oslo had shown that while many of those who did not react to tuberculin became ill with tuberculosis at an early stage of their training, only few cases developed among those found sensitive to tuberculin on admission. Prompted by this experience, Heimbeck began BCG vaccination of his tuberculin-negative nurses in 1926 and to-day he is still following up most of them. Among the probationers entering the school in the period 1924-1936 for a three-year training course, 668 were found positive to tuberculin on admittance, 501 were negative and BCG vaccinated, while 284 more negatives were not vaccinated. The following rates of morbidity and mortality were calculated for three groups per 1,000 observation years; for the positive group the rates were 12.4 morbidity, 0.0 mortality (22 cases of tuberculosis, all forms included, and no deaths), for the vaccinated 24.1 and 2.1 (35 cases and 3 deaths) and for the negative group 141.2 and 14.6 (97 cases and 10 deaths). Both morbidity and mortality appear very high in the latter group and Heimbeck stresses the fact that among the nurses who were vaccinated the incidence of tuberculosis has been reduced to one-sixth.

Several studies of this type, on selected groups highly exposed to infection and easy to control for a long period, were made in a never-ending effort to improve the conditions of the experiment and to gain new knowledge on the many problems involved. [Scheel (1935) and Holm (1941) on medical students, Nordwall (1944), Delachaux (1948), Genevriér and Maclouf (1948), etc., on nurses.]

R. G. Ferguson's (1946) observations on vaccinations of general hospital nurses and of sanatoria nurses showed that the protection given by BCG would apply as well to the groups with a high annual infection rate (sanatoria nurses : 71.8 per cent) as to the groups with a much lower annual infection rate (general hospital nurse : 11.8 per cent).

Comparison of the percentage of cases developing a tuberculous disease in the vaccinated and non-vaccinated groups shows a ratio of 1:6.5 for the more exposed nurses and of 1:4.5 for the less exposed nurses who had received BCG, such a marked reduction can hardly be attributed to mere chance or to the annual decline of the death and case rate in Canada.

In the years 1935-1938, Aronson in the United States started in 13 different Indian reservations, scattered from Arizona to Alaska, what was to become one of the most accurate studies on BCG. One thousand five hundred and fifty-one North American Indians were vaccinated with BCG and 1,457 were kept as controls. All the subjects chosen for the experiment were in the age group 1 to 20 and the division between those to be vaccinated and those to be followed up as controls was made quite at random. All the subjects were re-examined annually by tuberculin test and radiography. The statistical analysis of the material was made by Palmer (1946) of the U.S.

TABLE I
BCG vaccination in hospitals and sanatoria of Saskatchewan (R. G. Ferguson). (1934-1943)

Nurses in general hospital (yearly infection rate of 11.8 per cent)	Number of persons	Tuberculosis cases	Percentage with tuberculosis	Average years observed
Positive at admittance	478	5	1.05	2.43
Negative, not vaccinated	1,368	55	4.02	2.43
Negative, vaccinated	1,005	9	0.89	2.42
Nurses in sanatoria (yearly infection rate of 71.8 per cent)				
Positive on entrance	293	11	3.75	1.25
Negative, not vaccinated	113	18	15.9	1.06
Negative, vaccinated	203	5	2.46	1.07

Public Health Service. The specialist reading the x-ray films did not know to which group a given subject belonged. The two groups were found to be similar in age distribution, amount of exposure to tuberculous infection and completeness of the follow-up.

When the results of the Indian study were first published after 6 years of observation, there were 28 deaths due to tuberculosis among the controls as compared with only 4 such deaths among the BCG vaccinated. This is a rate of 3.4 against 0.4 per 1,000 person years, with a ratio of 1:7.7 in favour of the vaccinated. The total incidence of tuberculosis, that is, the sum of all the cases and all the deaths due to the disease, was 185 in the control group and 40 in the vaccinated group, that is, a rate of 24.3 as against 4.7 per 1,000 person years, or 1:5.2 in favour of the vaccinated.

in December 1942 and of the 368 pupils examined 105 were found tuberculin-negative, 130 tuberculin-positive after natural infection and 133 positive after BCG vaccination. About two months later, in January and February 1943, an influenza-like epidemic broke out among the school girls, beginning with several cases of erythema nodosum. After a renewed, thorough examination the source of infection was found to be a teacher of sciences who held classes in a damp, permanently blacked-out cellar. Some of the classes had not been in contact with the teacher in question so that out of the total 105 negative pupils, 94 had been exposed and 70 of them had become tuberculin-positive (74.5 per cent). Of these inverters 41 showed x-ray changes of the thoracic organs and 37 had a positive gastric lavage. In 11 cases, that is in 11.7 per cent of the exposed subjects, a progressive pulmonary

TABLE II
BCG vaccination among American Indians (J. D. Aronson and C. E. Palmer)

Number in group	NUMBER		PER 1,000 PERSON YEARS		
	Controls (2,550)	BCG (1,457)	Controls (8,977)	BCG (8,367)	Ratio BCG controls
Deaths from tuberculosis	28	4	3.4	0.44	1:7.7
Cases of tuberculosis	185	40	24.3	4.7	1:3.2

Furthermore, Aronson and Palmer mention a decrease in the number of cases of tuberculosis in the BCG group in the years following vaccination, while among the controls the morbidity rate remained fairly constant. According to the authors, this might indicate 'that the protection may be greater in the latter rather than in the earlier years after vaccination'.

Rosenthal, Blahd and Leslie (1945), in Chicago, to cite only one of their studies, kept under observation for more than ten years 1,204 infants who had been vaccinated during their first week of life and 1,213 who were kept as controls. Among the vaccinated three cases of tuberculosis developed and another child died of the disease, while among the non-vaccinated controls there were, in the same period of time, 23 cases of tuberculosis and 4 deaths.

Quite exceptional are the observations made by Hyge (1947) in a Danish school for girls, and his findings have been compared to those of a controlled laboratory experiment on humans. Following the discovery of an open case of tuberculosis among the pupils, the whole school population of the Aurehøj State School was x-rayed and tuberculin tested in November 1941 and again in February 1942. At this date 144 girls out of 200 tuberculin-negative reactors volunteered for vaccination and were subsequently found positive to a control tuberculin test. A new examination took place

tuberculosis developed, followed by death in one case. Among the 133 vaccinated 102 had been in contact with the infectious source and only two cases of tuberculosis developed (1.9 per cent). The only girl that had lost allergy after vaccination also suffered from a mild form of the disease. No other cases were found in 5 years of observation in this group. In the group of 130 who were originally tuberculin-positive, 105 had been exposed and four cases with positive gastric lavage were found.

Thus the efficacy of the vaccine has not only been proved beyond doubt on animals but we find that most of the experiments on human beings which can be subjected to statistical analysis give a percentage of protection of the vaccinated varying between 70 and 100 per cent (Irvine, 1949). This evidence has now been accepted universally and the use of vaccination in the fight against tuberculosis is no more a matter of faith as it was in Calmette's days. Even in Great Britain, where the attitude of some authors towards BCG has been highly critical (Wilson, 1947), vaccination will be made available on a national scale to particularly exposed groups under the provisions of the National Health Service Act (1948).

The question of whether BCG should be used only in groups particularly exposed to tuberculous infection and in populations with a high incidence of the disease

or if it should be given indiscriminately to all tuberculin-negatives whenever possible, still remains open for discussion. It is true that the evidence we now have on the effects of BCG has been gathered mostly from observations of highly exposed groups: nurses and medical students, North American Indians, children of tuberculous families, etc., and that we know much less about the epidemiological value of vaccination in populations with a low death rate from tuberculosis and a low infection rate.

In Denmark, for example, where the death rate for pulmonary tuberculosis has dropped to 22 deaths per 100,000 population in 1948 (The National Health Service of Denmark, 1948), vaccination is not only carried out on a wide scale but plans are being made to extend it further. On the other hand, some authors [like Myers (1948) in the U.S.] have expressed concern that the introduction of BCG would destroy the possibility of discovering new contagious cases of tuberculosis by repeated tuberculin surveys on a mostly negative population. The argument, however, has practical value only in countries where the control of tuberculosis has developed to such an extent that every single bacillary case can be traced and isolated immediately and where, moreover, there is little movement of the population requirements that are met with only in very few parts of the world to-day.

The situation described by Holm (1946) of the conditions on the Danish island of Bornholm, with a population of about 50,000, is a good example of how BCG can be useful as part of a good tuberculosis control system. After cattle tuberculosis had been eradicated from the island in the early twenties and all the open cases of the disease had been isolated, the percentage of negative reactors to tuberculin was the largest in Denmark, particularly in the younger generation. Nevertheless, cases of tuberculosis still developed and the age distribution was the same as in other parts of Denmark, with a peak in the 15 to 35 age group. The cases, mostly of a severe nature, occurred mainly in young negatives that left the island for some other part of the country and came back when they had contracted the disease. Vaccination of all negatives was begun in a systematic way in 1940 and since then there has been a marked reduction in the number of cases reported. This drop in the morbidity curve is particularly evident in the same 15 to 35 age group where the disease in previous years had had its richest harvest. And, as Holm states, this reduction must be ascribed to the extensive BCG vaccination in these age groups.

Although vaccination has been accepted in practice to such an extent that in some countries like Brazil, Czechoslovakia, France, Yugoslavia and Norway it has been made compulsory by law for certain population groups, there are still many improvements to be made and much information to be gained by further observation and research. The difference in the degree of protection provided by the vaccine, the possibility that protection may be different according to race, to the degree of exposure or to other known and unknown variables, and many other problems are of concern to clinicians and statisticians and spur them to continually new studies. In the United States, for example, a large research plan on BCG vaccination of school children with a comparable group of controls was started some years ago as part of a larger tuberculosis control experiment in a community of 100,000 population in Columbus (Georgia, 1947). Other large-scale studies of vaccination are in progress in Puerto Rico and in Finland, but results will be forthcoming only in some years.

The fact that vaccination can be safely used wherever necessary has been fully demonstrated by the mass campaigns now in progress in many parts of the world under the auspices of the International Tuberculosis Campaign. This programme, which began as a tuberculosis relief action by the Danish Red Cross in 1947 in Poland, Germany and Hungary, became an international effort in 1948 when it was joined by

Norwegian Relief for Europe, Swedish Red Cross, UNICEF (United Nations International Children's Emergency Fund) and the World Health Organization. As at 15th November, 1949, 17,600,000 persons had been tuberculin-tested and 8,200,000 BCG-vaccinated.*

Thus, after many years of study and trials, BCG vaccination has passed from the experimental phase to practical application in the field of tuberculosis control. The World Health Organization Expert Committee on Tuberculosis (1949), meeting in July 1949, has expressed itself in the following terms:

'It is considered that the number of individuals who would benefit from BCG vaccination on a large scale would be especially large in communities where tuberculous infection and disease are frequent. Mass-vaccination with BCG should, therefore, be recommended especially for communities with high tuberculous infection rates and mortalities. It is, however, recommended that even in countries where tuberculous infection and disease are relatively infrequent, vaccination be applied to individuals and groups with high degrees of exposure to tuberculosis, such as familial contacts and persons with occupational hazards.'

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* The following countries are participating in the I.T.C.—Europe: Austria, Czechoslovakia, Finland, Greece, Italy, Poland, Yugoslavia; Asia: India, Pakistan, Ceylon; Middle East: Egypt, Lebanon, Israel; North Africa: Algeria, Morocco, Tunisia. The I.T.C. Campaign is also scheduled for extension to other countries in these areas and in Latin-America in 1950, with a total goal of 50,000,000 to be tested and about 20,000,000 to be vaccinated.

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The Indian Medical Gazette Fifty Years Ago

ORGANIZATIONS FOR RESEARCH

(From the *Indian Medical Gazette*, February 1900, Vol. **35**, p. 63)

THE Tata and Iveagh gifts have stimulated a description of co-operative effort which constitutes a significant sign of the trend of modern thought and culture. How strange would the formula—a university for research or a research university—have sounded at the commencement of the present century. Towards its close the expression does not excite surprise, nay, it commands approval. The era during which culture implied a study of dead languages and abstract principles—so-called pure sciences—and in which a knowledge of Latin, Greek, mathematics, logic, metaphysics and philosophy was held to be the main, if not the sole object and business of a university, is being succeeded by an era, whose dawn is changing into day, in which it is recognized that the study of material objects and events—of nature in short—is the most worthy and useful and productive exercise of the mental faculties. The old universities have not succeeded in throwing off till recently the mantle of antiquity; but they are actively adapting themselves to the times by organizing faculties of science and introducing technical education—in agriculture and engineering for example. Medicine was the first and for a long time remained the only representative of this departure; but it is evidently not to retain that position in the more progressive seats of learning. The more conservative institutions—Oxford for instance—still conceive that language and philosophy are the proper subject-matter of

a superior education, and that the professions of divinity and law towards which they point and lead are the proper sphere of exercise for the higher faculties and more exalted intelligences. These notions are destined to be eclipsed in the near future by the growing conviction that realistic pursuits are superior to idealistic. On these grounds such organizations as the Royal Society and Jenner Institute in this country and the proposed Tata University in India, are entitled to special and strong commendation and support. The two first are achieving splendid results in the direction of physical and medical research, and the proposed new Research University in India which, I am glad to see the Government has taken up seriously, could not be laid upon better lines.

Why not a Veterinary Faculty?

Comparative pathology has taken such a high position in relation to the study of human diseases and their causes that the time has arrived when it ought to become part and parcel of a medical education. Disorders and injuries of the lower animal creation have hitherto been studied from a very low standpoint, namely, from the point of view of the value of stock and the loss of money and impairment of usefulness which sickness and maiming occasion. Our experience of plague has compelled us to pay close attention to the rat as a sharer in infection and agent of dissemination of that disease; the incidents of rabic disease have established a very close link between man and the dog and rabbit; and bacteriological investigations have revealed affinities between human and animal affections and infections which are not only of high scientific interest, but in many respects are of great practical moment in relation to prevention and cure. Comparative pathology has forced itself into general pathology as an integral and important part of the subject, and as such it is being taught in universities and medical schools. Why should the applied science and art which takes systematic account of the maladies of the lower animal creation and their prevention and treatment be excluded from a scheme or system of universal education and relegated to a separate and inferior corporation? I think that the time has come when veterinary education should be placed on a higher and better footing and should take its place beside medical education as a branch of scientific and technical university teaching.

An International Congress on Tuberculosis

A proposal has emanated from the 'National Association for the Prevention of Consumption and other forms of Tuberculosis' that an International Congress should assemble in London in the spring of 1950 under the presidency of H.R.H. the Prince of Wales, and an influential meeting is to be held on the 18th of this month for the purpose of making arrangements for the

same. The subject is one which cannot be too prominently or frequently held before the eyes of the medical profession and the public. An interesting and prolonged discussion is now taking place at the Royal Medical and Chirurgical Society on the open air treatment of tuberculosis. The proposed Congress will constitute a goal towards which thought and effort will be directed during the interval which will elapse between the present time and the period of its assembly, and the discussions which will take place will no doubt represent a large body of observation, research and experience of the most advanced and matured kind, and the conclusions arrived at will constitute a point of departure for renewed investigation and energy. The Berlin Congress fulfilled an excellent purpose in focusing existing knowledge, and the London Congress ought to exhibit a very substantial addition to the large and interesting mass of information presented at the former gathering.

Tuberculosis in India

Dr. A. Crombie, who attended the Berlin Congress as a delegate for India, has drawn up a very excellent report on the proceedings of the assembly and compiled some useful notes on the prevalence of tuberculous disease in India. These latter are summarized in an article published in the issue of the *British Medical Journal* for October 28th (pp. 12 and 13) to which I would direct special attention. Tuberculosis is one of the most striking and practically important illustrations of that intimate association of human and comparative pathology to which I have already alluded.

The War in South Africa

The tidings which have reached this country indicate that the arrangements which have been made for the treatment of the sick and wounded are working well and leave nothing to be desired. The Army Medical Department has risen to the occasion, and so far as can be judged, acquitted itself with commendable despatch and thoroughness. No considerable amount of sickness appears to have occurred among our troops, though the Boers, whose medical and sanitary arrangements seem to be of very rudimentary and defective kind, are said to be suffering from dysentery and scurvy. Enteric fever is known to be very rife in South Africa, and the effect of the antityphoid inoculations, which some 70 per cent of our soldiers have undergone, will be watched with eager interest. As the fact of inoculation has been noted on each man's medical history sheet, which will also display all his admissions into hospital and their cause, reliable statistics on the protective power of these proceedings should be forthcoming. At present the figures which have been collected, though on the whole favourable, are by no means decisive.

The Annual Meeting of the British Medical Association

The arrangements for the Ipswich meeting of the British Medical Association in August are being made and published. The locality is at that time of year a charming one as regards scenery and air, and the town and its neighbourhood abound in sights of beauty and interest. I hope that many officers on leave from India will find their way to the meeting and assist by their presence and work in contributing to the success of the section of tropical diseases. A new section for the Navy, Army and Ambulance has been organized which, in view of past discussions and passing events, ought to be a strong one.

K. McL.

7th December, 1899.

Current Topics, Etc.

Physical Treatment of the Hæmiplegic Patient in General Practice

By H. DINKEN

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 30th April, 1949, p. 1255)

THE aims of physical treatment in general are to improve motor function, increase functional capacity, prevent or correct deformity and provide for the overall adjustment of the hæmiplegic patient to the demands of daily life.

Treatment should be instituted as soon as possible. In the majority of cases it can be started within the first week following onset. There are few medical contra-indications to early treatment in most cases, especially to passive movement of the involved extremities daily, which is particularly important. The fear of producing extension or reactivation of the cerebral vascular lesion is apparently without justification, as indicated by clinical experience.

Much of the crippling deformity seen in this group of patients can be avoided by early adequate treatment. The common occurrence of contractures about the shoulder joint, the so-called 'frozen shoulder', can be avoided as can the flexion deformities of wrist and fingers, the externally rotated hip, the flexed knee and the dropped foot.

There are numerous effective agents and techniques available to the practitioner in the management of his hæmiplegic patient.

There are three principal indications for the use of heat in hæmiplegia. They are the presence of pain, spasticity and oedema. Any form of heat, therapeutically active, will suffice, although many patients seem to fare better with moist heat in the form of hot packs. Heat should be followed by massage, especially if oedema is present. Aside from these limited indications, heat and massage are of little value. It is infinitely more important to devote time to the functional programme of retraining and movement re-education.

There is a limited field of usefulness for low frequency currents, such as the interrupted galvanic. Occasionally, when flaccidity persists, electrical stimulation will serve to maintain tone and prevent atrophy. It may also be of value in the initiation of the

programme of movement re-education. Spastic groups should not be stimulated, since this would tend to accentuate existing muscle imbalance.

Movement re-education is of prime importance. It must be done carefully, indicating to the patient origins and insertions and type of movement desired. Often, reciprocal motion or use of the good extremities first will be of help. It is surprising how very frequently movement is possible even though the patient, on direct questioning, denies ability to use the part. Walking re-education should be graduated as progress is made. As a general rule, when the quadriceps can function against gravity and there is sufficient stability at the hip and ankle, the patient should be gotten up. Every attempt should be made to make the patient ambulatory as soon as possible. Some mechanical aid may be required, at first, in the walking programme. Postural and balance training should be incorporated in the programme.

Pulley exercises are of great value in the treatment of the hæmiplegic patient. They offer reciprocal motion which is invaluable in re-learning. Secondly, they permit adequate stretching of contractures, such as occur in the shoulder. The patient is responsible for the movement and hence does not fear the pain of passive stretching done by some one else. An additional increment of several degrees of motion can frequently be obtained.

Appliances are often indicated. Splints may be made of plastic or of padded plaster shells. They are especially useful in prevention of contractures of the wrist and fingers. A short leg brace with a 90 degree stop at the ankle may be required to correct a persistent drop foot which interferes with walking. The use of a foot board early, to keep weight of the bed clothes from the lower extremities, is of value. Sandbags or pillows may be used to maintain normal alignment in bed.

Occupational therapy utilizing the arts and crafts provides many activities designed to improve muscle strength, co-ordination and endurance. These activities are also valuable in providing reciprocal motion and movement re-education. Properly prescribed and carried out, it is invaluable as a morale booster and as an outlet for the patient's useless anxiety. Remember, action absorbs anxiety; however, it is more important for the patient to learn left-handed writing or shoe string tying than it is to weave a rug. Activities must be provided that are both diversional and useful.

Para-Aminosalicylic Acid (P.A.S.) in Pulmonary Tuberculosis

By M. M. NAGLEY

and

M. H. LOGG

(Abstracted from the *Lancet*, i, 28th May, 1949, p. 913)

THE compound p.a.s. was first synthesized by Seidel and Bittner in 1902 as a white powder decomposing at 140°C.-150°C. into meta-aminophenol, and it was one of a series of salicylic-acid products investigated by Lehmann. Bernheim showed that sodium salicylate would increase the oxygen uptake of tubercle bacilli, and he suggested that it, or its derivatives, may be metabolites of that bacillus. He also found that, whereas salicylic and benzoic acids had this property, their homologues were inactive. Lehmann reported in this journal that, of more than fifty derivatives of benzoic acid he had studied, the most actively tuberculostatic one was p.a.s.

CLINICAL METHODS

From using a suspension of the crude acid, we have now turned almost completely to the sodium salt of

p.a.s. in solution for administration by mouth, which has been the main route employed in treatment. It was thought that this sodium salt had less unpleasant side-effects than the crude acid.

DISCUSSION

The tuberculostatic action of p.a.s., judged by the experimental work and the bacteriological findings in sanatorium practice, cannot now be doubted. The mode of action that p.a.s. seems to exert on the host, as shown by the fact that the patient's feeling of well-being, the antipyretic effect, and the improvement in the general condition are the most constant results of treatment.

In practice, the low toxicity of p.a.s. and its apparent lack of any tendency to produce resistant strains give it advantages over streptomycin in the treatment of exudative lesions, more particularly where the infecting strain is streptomycin-resistant and in the cases—fortunately becoming rarer—where streptomycin has produced toxic effects in the central nervous system.

The general principles of p.a.s. treatment in pulmonary tuberculosis are the same as with other chemotherapeutic agents and can be summed up as follows: except in the miliary forms of tuberculosis, chemotherapy should be used to achieve a definite goal; this is not necessarily the 'cure' of the disease, as shown by sputum conversion, radiological healing, etc., but is merely a point at which the next stage of treatment—collapse therapy, or major pulmonary surgery—can be carried out. The patient's natural powers of 'resistance' may be enhanced so that further improvement can be expected on continued rest in bed.

Used with this target in mind, we have found that p.a.s. can be a valuable auxiliary measure in the treatment of acute pulmonary tuberculosis, and that many collapse measures could be performed in cases which, without p.a.s., would either have deteriorated or have improved to a degree at which collapse measures were still impracticable.

SUMMARY

An analysis has been made of 37 cases of active pulmonary tuberculosis treated with p.a.s. at the Grove Park Hospital in 1947-48.

From these and other cases it seems that the main value of p.a.s. in pulmonary tuberculosis is in the acute exudative type of disease, particularly in all toxic febrile patients.

Such effects as reduction in temperature, fall in e.s.r., gain in weight, and a feeling of well-being occur long before radiological improvement can be demonstrated, and, once present, they remain during treatment.

Patients with acute post-operative and other types of acute pulmonary tuberculosis should not be denied streptomycin, but the value of p.a.s. in such cases, either in conjunction with streptomycin or after its use, should be realized, though p.a.s. must not be looked on as a substitute for the accepted forms of non-chemotherapeutic treatment.

Hiccup

(Abstracted from the *Lancet*, i, 14th May, 1949, p. 830)

HICCUPING is sometimes tiresome and always purposeless. It consists of intermittent spasmodic contraction of the diaphragm accompanied by closure of the glottis; and the familiar 'hic' sound is due to sudden inspiration terminated abruptly as the vocal cords come together. Hiccups may be a reflex response to stimulation of afferent pathways to centres in the cord or medulla; or they may arise from stimulation of the centres themselves, or of the afferent pathways, of which the chief is the phrenic nerve. At the same time

there is sometimes spasm of the intercostal and accessory muscles of respiration, which are controlled by the respiratory centre.

Over two hundred different treatments have been proposed. Homely therapy is often as effective as any—for example, such stimuli as a slap on the back (which should be sudden and surprising enough to cause initial resentment), traction on the tongue, tickling the nares, painting the uvula with iodine, inhaling smelling-salts, and drinking neat whisky. Both holding the breath and deep breathing have their advocates; and inhaling carbon dioxide is sometimes effective. When a gastric cause is suspected, alkalis, aromatic oils, and carminatives may be tried; and occasionally aspiration or lavage of the stomach or induction of vomiting may be warranted. For the relief of abdominal distension, neostigmine and vasopressin have been used. With the distressing post-operative hiccup, action is imperative; and here the usual measures often disappoint. Bromides, barbiturates, opium derivatives, and hyoscine are commonly used, and even general anaesthesia has been recommended; a firm abdominal binder will help to minimize fatigue. In some cases with dehydration Peet has found the liberal administration of intravenous fluids effective. Antispasmodics may be tried—for example, atropine, or amyl nitrite, which has been the subject of an enthusiastic report. Amphetamine, which is known to relax the smooth muscle of the gastrointestinal tract, has been used with success in two cases; while another antispasmodic, benzyl benzoate, has been employed as a 20 per cent solution in doses of 2 ml. by mouth four-hourly. Arguing on the analogy of the effects of cinchona alkaloids on striated and on cardiac muscle, Bellet and Nadler have lately used quinidine for intractable hiccup. Of 9 cases where the customary methods had failed, quinidine arrested the paroxysms in 6, and was partly successful in a further 2. The dose recommended is gr. 9 by mouth or intramuscular injection, if necessary, repeated 2 to 3 times at hourly intervals.

The possibility of treatment by interrupting the phrenic nerve was recognized more than a century ago; in 1833 Shortt, of Edinburgh, succeeded in two cases by blistering the surface of the neck over the origin and course of the nerve. Shortt's review shows how little has been added to our knowledge in the past hundred years. Since then interruption of the nerve has been achieved in various other ways, including digital compression of the cervical portion between the heads of the sternomastoid muscles, galvanic and faradic currents to the neck, freezing with ethyl chloride, traction on a ligature round the nerve, and procaine block. If all else fails, the nerve can be crushed. Weeks reports the application of this treatment to a case where hiccup was apparently due to right-sided diaphragmatic pleurisy, and only the nerve on that side was crushed; he suggests that the diaphragm should be screened in an attempt to determine which side is at fault. Rarely even bilateral phrenicotomy fails; and then the hiccup may be due to spasm not of the diaphragm but of the intercostal and accessory muscles of respiration.

Absorbable Hæmostatics

(From the *British Medical Journal*, i, 11th June, 1949, p. 1044)

SURGEONS have long been haunted by the spectre of hæmorrhage from inaccessible vessels. Much has been done by good lighting and exposure of the field of operation to reduce this danger, and much can be done by local pressure maintained with patience for many minutes, if necessary. But in the rare case, even in experienced hands, packs or hæmostats have had to be left in wounds, prolonging the period of danger for the patient and of worry for the surgeon. If they are left for more than 24 hours, there is grave risk of

infection, while their removal may restart the hæmorrhage. The arrival of absorbable hæmostatics has abolished these dangers, and several surgeons have reported on their usefulness.

Of the four substances in use oxidized cellulose, fibrin foam and gelatin sponge have been developed in the U.S.A., and calcium alginate is a British product. All appear to be very effective hæmostatics, and comparisons of the first three have shown them to be about equal in this capacity. Oxidized cellulose, however, has the disadvantages that it is highly acid and so inactivates thrombin and penicillin, and it does not adhere so firmly as does gelatin; moreover, it has to be sterilized chemically with bacteriological control. There appears to be little difference in the efficacy of fibrin foam and gelatin sponge, but fibrin is more complicated to use and to sterilize and is more easily broken up. Gelatin sponge, which can be sterilized by dry heat, is inexpensive, non-antigenic, non-irritant, and does not inactivate antibiotics or thrombin. Its efficiency as a hæmostatic has been shown by its use to cover actual defects in large veins and for wounds of the heart. Large nephrotomy incisions, extending into the renal pelvis, healed well without leakage of urine after packing with gelatin foam. A further application of absorbable hæmostatics is for packing large cavities which have rigid walls. A notable example is the use of gelatin foam in the pleural cavity after pneumonectomy. Provided too large amounts are not used, dogs and rats tolerate it well. It stabilizes the mediastinum and reduces greatly the amount of fibrinous exudate, and at the same time it does not interfere with repair. If infection is present, the gelatin is rapidly liquefied and does not aid the infective process. This experimental work suggests that gelatin foam will have a valuable place in thoracic surgery.

Calcium alginate gauze has been shown to be a useful hæmostatic in liver wounds in cats, and it has the merit that it can be sterilized by autoclaving. It appears to be well tolerated in the tissues, and no untoward reactions were observed. There can be little doubt that the use of these and other absorbable hæmostatics will increase especially for arresting troublesome hæmorrhage.

Reviews

HUMAN BIOCHEMISTRY.—By Israel S. Kleiner, Ph.D. Second Edition. 1948. The C. V. Mosby Company, St. Louis. Pp. 649. Illustrated. Price (not mentioned)

This useful book presents an account of the biochemical processes in the healthy human body in a manner which is neither too elementary nor too advanced. Wherever necessary, the author points out the clinical aspects of biochemistry and in addition there is an informative chapter at the end of the book on clinical application of biochemical tests. This edition includes much new material, and a new chapter, 'chemical structure in relation to biological phenomenon', has been added.

R. N. C.

NUTRITION.—By Lieut.-Colonel Barkat Narain. Foreword by the Hon. Rajkumari Amrit Kaur, Minister of Health, Government of India. Second Edition. Illustrated, revised and enlarged. Pp. 75. Price, Re. 1-8

We welcome a new edition of this book. Obviously it has been gaining in popularity; it has already been translated in Hindi, and it is proposed to issue a Gurmukhi edition. It talks in simple language com-

position of food, what food to buy, how to purchase it, how to prevent wastage, values of different food-stuffs, and symptoms that may arise from food deficiencies. It also gives samples of balanced diet and of diets for children and expectant mothers, indoor workers and labourers. The book which is primarily meant for the general public should be widely read and used in our households.

R. N. C.

RADIOTHERAPY AND CANCER.—By A. G. C. Taylor, M.R.C.S., L.R.C.P., D.R., F.F.R., J. Lassetter, M.B., Ch.B., D.R., and T. K. Morgan, M.B., M.R.C.S., D.M.R.(T.). 1948. H. K. Lewis and Co., Limited, London. Pp. 81. Price, 7s. 6d.

In the treatment of cancer surgery and radiotherapy hold the field, but they are largely complementary. Some tumours are suitable for operation, in others good results can be obtained by radiotherapy, while in still others a combination of both methods is the best. Moreover, radiotherapy can be used as a palliative in a large proportion of cases. This handy little book gives the essential points in this form of treatment for guidance of specialists and general practitioners. In the first part the authors briefly explain the physics of radiotherapy, radiobiology, selection of cases and methods of treatment. In the second part they give their views as to how cancer should be treated, depending on the site of origin, the extent and histology. Surgery is mentioned when this is an alternative treatment. The booklet will enable physicians, surgeons and general practitioners to understand the radiotherapists' point of view and help them in advising their patients.

R. N. C.

SYNOPSIS OF PSYCHOSOMATIC DIAGNOSIS AND TREATMENT.—By Flanders Dunbar, M.D. et al. 1948. The C. V. Mosby Company, St. Louis. Pp. 501. Illustrated. Price (not mentioned)

Recent investigations tend to show that emotions and psychiatric states play an important rôle in the causation of many bodily illnesses, and that such patients are best managed if a psychosomatic approach is made in their treatment. This is especially true in certain types of cardiovascular and gastro-intestinal diseases, metabolic and endocrine disturbances, asthma, etc. In this synopsis Dr. Dunbar and his collaborators discuss the psychological aspects of diseases with reference to ætiology and treatment, quoting many case histories. 'What psychosomatic medicine does is to turn the methods of psychological medicine to use on the hitherto so-called purely organic illnesses. It subtracts nothing; it adds the techniques of anatomic, chemical and physical research, and anatomic and physiologic clinical investigation.' The book shows a trend in modern medicine which may go to the elucidation of many clinical problems.

R. N. C.

THE AMERICAN NURSES' DICTIONARY. THE DEFINITION AND PRONUNCIATION OF TERMS IN THE NURSING VOCABULARY.—By A. L. Price, B.S., R.N. 1949. W. B. Saunders Company, Philadelphia and London. Pp. 656. Price, 19s.

This excellent dictionary is a useful addition to medical literature and will be consulted by nurses and medical men alike. Perhaps it will go a little beyond a nurse's need who does not require the 25,000 words defined in it.

The paper, the printing and the binding are excellent. A thumb index is added.

A few faults are unavoidable in a first edition of any book. One of them is 'chair' on page 115: It comes after cervix and before cesium. Obviously, it is out of place and not necessary in a medical dictionary at all.

it is recommended that digitalin for use in injectable preparations should be standardized biologically. Research has mainly been directed towards: (i) Finding Indian substitutes for official drugs and preparations, (ii) problems of deterioration in potency, (iii) improvements of existing methods of analysis and standardization, (iv) general problems, comprising blood transfusion materials, hydrolysates, snake venom, and proteolytic activity in relation to diseases (e.g. tuberculosis and typhoid). Forty-eight scientific papers have been published and others are awaiting publication.

REJECTED PRODUCTS

It may be concluded that in detecting and arresting exploitation, in maintaining high standards in the industries, in its original research, training personnel, and in public health propaganda, the Laboratory has already worthily served the new India.

It is evident that the vision of the founder and first director of the Laboratory, Colonel Ram Nath Chopra, F.R.S., has been the inspiration of his worthy pupil and successor, Dr. B. Mukerji, to whose energies the progress now recorded is largely attributable.

Correspondence

WASSERMANN REACTION

SIR,—The following case is reported with the idea of knowing the experience of others.

Blood of a patient admitted to the Tata Main Hospital was sent on 6th January, 1950, for WR and Kahn tests. Kahn test turned out (+ + + +) and WR showed anticomplementary result. A fresh sample of blood was called for and repeated on 10th January, 1950, with the same finding. For the third time on 13th January, 1950, a fresh sample of blood of the patient was collected in the Laboratory and the tests when repeated showed exactly the same results.

In order to get over this persistent anti-complementary tendency, for the fourth time on 17th January, 1950, blood was collected and WR done by two methods. Sachs' process as suggested by S. D. S. Greval in his book on 'Complement Fixation' and by the method recommended in the *Journal of Laboratory and Clinical Medicine*, Vol. 31, No. 9, September 1946, page 1037.

Of these two methods, by the Sachs' method it was possible to declare the case as strongly positive.

Yours faithfully,
T. V. SWAMY, M.B., B.S.,
Senior Pathologist,
Tata Main Hospital.

UNUSUAL CURE OF ANGINA PECTORIS AFTER VIRUS DISEASE

SIR,—I read with interest the note by Dr. K. S. Hossain on 'Unusual cure of angina pectoris after virus disease', in your issue of November 1949, p. 502. Many years back I read before the then Kathiawar Medical Society at Rajkot notes of a case of whooping cough which got cured after the patient developed an attack of measles. I gave my notes the heading 'Antagonism in disease'. The patient was a male child of 4 years age suffering from whooping cough. He developed measles of the seventh day after he started whooping cough. The relief from whooping cough was very striking, the fits of coughing and subsequent vomiting being abolished from the third day of his having measles.

In the *Journal of the American Medical Association* for 3rd September, 1949, p. 24, Dr. Nathan Gorin of Boston has reported three cases of chronic and intractable asthma in which there was relief of asthma with the appearance of jaundice due to (1) infectious hepatitis, (2) presumable homologous serum hepatitis and (3) metastatic adenocarcinoma of the liver.

One could only speculate on the cause or causes of such a dramatic relief in cases in which, it seems, one disease condition elbows out another.

Yours faithfully,

K. V. THAKKAR,
L.M. & S. (Bom.).

MEDICAL BUILDING,
BHAVNAGAR,
5th February, 1950.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL BARKAT NARAIN, Director of Health Services, Delhi Province, is placed on deputation ex-India with effect from the 3rd December, 1949 (afternoon).

Major M. S. Chandha, Deputy Director of Health Services, Delhi Province, is appointed to officiate as Director of Health Services, Delhi Province, with effect from the 3rd December, 1949 (afternoon), *vice* Lieutenant-Colonel Barkat Narain.

Dr. K. V. Venkataraman, an Officer of the Medical Research Department, is appointed temporarily as Officer on Special Duty, in the Office of the Serologist and Chemical Examiner to the Government of India, Calcutta, with effect from the afternoon of the 16th December, 1949.

LEAVE

Dr. C. B. D'Silva, Officiating Assistant Director, Central Research Institute, Kasauli, is granted earned leave for 62 days with effect from the 2nd December, 1949.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

The preparation of reprints entails rearranging the type, so that there is often a delay of a month or more, after the publication of the *Gazette*, before the reprints are ready. If reprints are not received within two months of publication of the *Gazette*, contributors should write to the Publishers.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

CONTENTS

	Page		Page
ORIGINAL ARTICLES			
Streptomycin in Tick-borne Relapsing Fever of Kashmir. <i>By S. Narain, Colonel, and S. L. Kalra, Major</i> ..	87	DRUGS RULES, 1945 ..	113
Echinococcal Cyst of Broad Ligament. <i>By H. N. Ray, M.B., F.R.C.O.G. (Lond.)</i> ..	88	MINUTES OF THE MEETING OF THE UNITED PROVINCES MEDICAL COUNCIL, HELD AT LUCKNOW ON TUESDAY, 29TH NOVEMBER, 1949 ..	113
Pneumoperitoneum in the Study of Hepatic Abscess. <i>By H. B. Lal, Lieutenant-Colonel, I.A.M.C.</i> ..	90	NEW DESIGN AMBULANCE PLANE ..	114
Generalized Cysticercosis Cellulosæ. <i>By C. J. Dave</i> ..	92	LONDON RED CROSS EXHIBITION ..	114
Some Constituents in Normal Blood in Central India. Serum proteins, serum albumin, serum globulin and serum non-protein nitrogen. <i>By S. H. Gokhale and R. J. Lokre</i> ..	94	GYMNASIUM AIDS HOSPITAL PATIENTS ..	115
Creeping Myiasis in Man. An unusual case. <i>By S. M. Ghosh</i> ..	96	FLUORESCENT HOSPITAL BED ..	115
Epidemic Dropsy complicating Pregnancy. <i>By K. P. Bhadury, M.B.</i> ..	98	MOST MODERN PHYSICAL MEDICINE DEPARTMENT ..	116
Typhus in Myllem State Area, Shillong. <i>By I. B. Roy, L.M.P., D.T.M.</i> ..	99	QUARANTINE RESTRICTIONS ..	116
A MIRROR OF HOSPITAL PRACTICE		THE 11TH MAHARASTRA AND KARNATAK PROVINCIAL MEDICAL CONFERENCE, DHARWAR. 6TH, 7TH AND 8TH OF MAY, 1950 ..	116
A Case of Xeroderma Pigmentosa in a Sinhalese. <i>By G. H. Cooray, M.D. (Lond.), M.R.C.S., D.T.M. & H. (Eng.), and P. A. P. Joseph, M.B., B.S. (Ceylon)</i> ..	101	THE WORLD MEDICAL ASSOCIATION ..	116
Effect of Fibrolysin and Antithyroidin on Raynaud's Disease (after Sympathectomy). <i>By S. K. Datta, B.Sc., M.B., and P. C. Thakurta</i> ..	102	NEW SUB-MINIATURE VALVES ..	117
Brief Notes on Two Cases of Scrub Typhus Fever with Unusual Neurological Signs. <i>By Captain G. S. Rao, M.B., B.S.</i> ..	103	W.H.O. IN THE FIELD: WIDESPREAD SERVICES IN OPERATION ..	117
THERAPEUTIC NOTES		<i>The Dutch Archives of Surgery</i> ..	117
Notes on Some Remedies. XXXIII. Dehydration and its treatment. <i>By R. N. Chaudhuri, M.B., M.R.C.P., T.D.D.</i> ..	105	OUTBREAK OF Q FEVER IN LONDON ..	118
EDITORIALS		MALARIA CONTROL IN THE BRITISH COLONIES ..	118
Para-aminosalicylic Acid: PAS ..	107	FIFTH SESSION OF W.H.O. EXECUTIVE BOARD. REPORT ON S.-E. ASIA HEALTH PROBLEMS ..	118
Polio Yet Again ..	108	W.H.O. BOARD URGES DEVELOPMENT OF REGIONAL HEALTH ACTIVITIES ..	119
MEDICAL NEWS		FIFTY YEARS AGO	
ANTITETANUS INOCULATION ..	108	RECENT ITALIAN WORK ON MOSQUITO MALARIA (<i>Indian Medical Gazette</i> , March 1900, Vol. 35, p. 101) ..	119
INDIA SETS UP POPULATION INSTITUTE ..	108	CURRENT TOPICS, ETC.	
WORLD HEALTH ORGANIZATION FELLOWSHIPS ..	108	CONTINUOUS INTRAVENOUS INJECTION OF TYPHOID VACCINE IN TREATMENT OF CERTAIN OPHTHALMIC DISEASES ..	121
HOW THE DEAF MAY 'HEAR THROUGH THEIR FINGERS' ..	109	CURE OF CHRONIC VIVAX MALARIA WITH PENTAQUINE. <i>By L. T. Coggeshall and F. A. Rice (Journal of the American Medical Association, Vol. 139, 12th February, 1949, p. 437)</i> ..	122
DEATH RATE IN THE UNITED STATES ..	109	EWING'S TUMOUR ..	122
SIGNING OF AN AGREEMENT BETWEEN W.H.O. AND THE GOVERNMENT OF CEYLON ..	111	THE DISC SYNDROME: RESULTS OF THE CONSERVATIVE CARE OF PATIENTS WITH POSITIVE MYELOGRAMS ..	122
EXPERTS ADVISE ON TRAINING MEDICAL AND HEALTH PERSONNEL. GREATER EMPHASIS ON SOCIAL AND PREVENTIVE MEDICINE NEEDED ..	111	THE USE IN CHILDREN OF PROCAINE PENICILLIN WITH ALUMINIUM MONOSTEARATE. <i>By J. L. Emery, et al. (British Medical Journal, i, 25th June, 1949, p. 1110)</i> ..	123
AFGHANISTAN MONARCH VISITS W.H.O. GENEVA HEADQUARTERS ..	111	A SIMPLE WEIGHT-REDUCING DIET. <i>By H. L. Marriott (British Medical Journal, ii, 2nd July, 1949, p. 18)</i> ..	123
INDIA AIDS BURMA TO FIGHT SMALLPOX ..	112	CORTISONE IN THE TREATMENT OF RHEUMATISM (<i>British Medical Journal, ii, 2nd July, 1949, p. 24</i>) ..	124
TURKEY TO INTENSIFY FIGHT AGAINST TUBERCULOSIS ..	112	ANTIBIOTICS IN PRIMARY ATYPICAL PNEUMONIA (<i>Lancet, ii, 16th July, 1949, p. 110</i>) ..	124
W.H.O. EXPERTS RECOMMEND MEASURES IN WORLD-WIDE SHORTAGE OF NURSES ..	112	CLINICAL INTOXICATION WITH POTASSIUM: ITS OCCURRENCE IN SEVERE RENAL INSUFFICIENCY. <i>By M. M. Keith and H. B. Burchell (Journal of the American Medical Association, Vol. 140, 11th June, 1949, p. 559)</i> ..	124

(Continued on page 86)

	Page
POISONING FROM ANILINE MARKING ON DIAPERS (<i>Journal of the American Medical Association</i> , Vol. 140, 25th June, 1949, p. 684)	125
PERORAL ADMINISTRATION OF UNDECYLENIC ACID IN PSORIASIS. By H. H. Perlman and I. L. Milberg (<i>Journal of the American Medical Association</i> , Vol. 140, 9th July, 1949, p. 865)	125
DANGERS OF INTRATHECAL MEDICATION. By G. Wilson et al. (<i>Journal of the American Medical Association</i> , Vol. 140, 30th July, 1949, p. 1076)	125
SYNERGISTIC ACTION OF PENICILLIN AND STREPTOMYCIN ON <i>Endamæba histolytica</i> Cultures. By H. Seneca et al. (<i>Journal of the American Medical Association</i> , Vol. 140, 30th July, 1949, p. 1120)	125
CHLOROQUINE AND HEPATIC AMOEBIASIS (<i>Medical Journal of Australia</i> , Vol. II, 9th July, 1949, p. 63)	125
ISOPROPYLEPINEPHRINE AND BRONCHIAL ASTHMA (<i>Medical Journal of Australia</i> , Vol. II, 30th July, 1949, p. 173)	126
PARACHOLERA (<i>Medical Officer</i> , Vol. 81, 4th June, 1949, p. 232)	126
ORAL ADMINISTRATION OF AUREOMYCIN IN THE TREATMENT OF GONORRHOEA. By C. H. Chen et al. (<i>Urologic and Cutaneous Review</i> , Vol. 53, July 1949, p. 394)	127
THE PRESENT STATUS OF THE TREATMENT OF THYROTOXICOSIS. By W. H. Beirwaltes and C. C. Sturgis (<i>Practitioner</i> , Vol. 162, June 1949, p. 486)	127
THE BACTERIOLOGY OF FOOD POISONING. By G. S. Wilson (<i>Practitioner</i> , Vol. 162, June 1949, p. 445)	127
TICK-BORNE RELAPSING FEVER IN KASHMIR. By K. N. A. Rao and S. L. Kakra (<i>Current Science</i> , Vol. 18, July 1949, p. 249)	128
THE EFFECT OF CHLOROQUINE DIPHOSPHATE ON MALARIA SPLENOMEGALY. By D. A. Berberian and E. W. Dennis (<i>American Journal of Tropical Medicine</i> , Vol. 29, July 1949, p. 463)	128
METHODS OF PINWORM DIAGNOSIS. By P. C. Beaver (<i>American Journal of Tropical Medicine</i> , Vol. 29, July 1949, p. 577)	128
'P-A-S' (PARA-AMINO-SALICYLIC ACID) (<i>Medical Review</i> , Vol. 43, July 1949, p. 106)	129
PLAGUE. By Dr. Georges Blanc (Reproduced from W.H.O. Special Features, No. 4)	129
TEMPORARY RELIEF OF ASTHMA BY JAUNDICE. By N. Gorin (<i>Journal of the American Medical Association</i> , Vol. 141, 3rd September, 1949, p. 24)	130

REVIEWS

THE CLINICAL APPRENTICE: A GUIDE FOR STUDENTS OF MEDICINE. By John M. Naish, M.D. (Cantab.), M.R.C.P., and John Apley, M.D. (Lond.), M.R.C.P. 1948	130
--	-----

	Page
CARDIOVASCULAR DISEASE IN GENERAL PRACTICE. By Terence East, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Third Edition. 1949	130
TUBERCULOSIS INDEX AND ABSTRACTS OF CURRENT LITERATURE. QUARTERLY, JUNE 1949, VOL. 4, NO. 2	130
SYNOPSIS OF PÆDIATRICS. By John Zahorsky, A.B., M.D., F.A.C.P. Assisted by T. S. Zahorsky, B.S., M.D. Fifth Edition. 1948	130
A TEXTBOOK OF MIDWIFERY. By Wilfred Shaw, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G. Third Edition. 1949	130
A HISTORY OF THE HEART AND THE CIRCULATION. By Fredrick A. Willius, M.D., M.S. (in Med.), and Thomas J. Dry, M.A., M.B., Ch.B., M.S. (in Med.). 1948	131
WARD ADMINISTRATION AND CLINICAL TEACHING. By Florence Meda Gipe, M.S., R.N., and Gladys Sellew, Ph.D., R.N. 1949	131
THE NATIONAL HEALTH SERVICE. By Charles Hill, M.D., and Jock Woodcock. 1949	131
OPERATIONS OF GENERAL SURGERY. By Thomas G. Orr, M.D., New (Second) Edition. 1949	131
AN ATLAS OF AMPUTATIONS. By Donald B. Slocum, M.D., M.S. 1949	131
BASIC SURGERY. By Aniya Kumar Sen, M.D. (Cal.), D.P.H. (Lond.), F.R.C.S. (Eng.). First Edition	131
A TEXTBOOK OF SURGERY. By American Authors. Edited by Frederick Christopher, B.S., M.D., F.A.C.S. New (Fifth) Edition. 1949	131
DOCUMENTA OPHTHALMOLOGICA—ADVANCES IN OPHTHALMOLOGY. Edited by F. P. Fischer, A. J. Schaeffer and Arnold Sorsby. Vol. III. 1949	131
THE PRACTICE OF REFRACTION. By Sir Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Ph.D., M.D., F.R.C.S., Hon. D.Sc. (North Western). 1948	132
OPHTHALMIC MEDICINE. By J. H. Duggart, M.A., M.D. (Cantab.), F.R.C.S. (Eng.). 1949	132
CLINICAL PERIMETRY. By H. M. Traquair, M.D., F.R.C.S. (Edin.). Sixth Edition. 1949	132

BOOK NOTICE

SOUVENIR OF THE 22ND ANNUAL CONFERENCE, 1950	132
--	-----

BOOKS RECEIVED

CORRESPONDENCE

SUDDEN DEATH OF BABIES	133
CLINICAL HYDROPHOBIA WITHOUT CONTACT WITH RABIES TRANSMITTING ANIMAL	133
M.D. AND M.S., BOMBAY	133

SERVICE NOTES

Original Articles

STREPTOMYCIN IN TICK-BORNE RELAPSING FEVER OF KASHMIR

By S. NARAIN

COLONEL

and

S. L. KALRA

MAJOR

PROLONGED observations on arsenic therapy in relapsing fever of Kashmir have shown that 97 per cent of the cases were cured with 1.0 to 1.6 g. of NAB in divided doses. The rest of the cases either did not respond to it or relapsed within a month. Penicillin was tried and found ineffective. The use of streptomycin in this disease is not mentioned in literature, although Levaditi and Vaisman (1947) recorded its favourable effect on *S. duttoni* in laboratory experiments. No clinical trials, however, have been recorded so far in literature. In searching for an alternative therapy, therefore, it was proposed to try the anti-biotic. Eighteen cases have been treated so far and their clinical features and results are given below.

Clinical Features

The cases treated with streptomycin were typical of the diseases in Kashmir, and their symptoms were briefly as follows. The onset was with chill and the crisis with a little sweating. The first paroxysm was accompanied by headache, mild or severe, with generalized aches and pains all over the body or localized to the lumbar region of the back or the calf muscles. These symptoms abated during the apyrexial interval but were aggravated in relapses. The paroxysm lasted from 1 to 7 days. The relapses were generally of shorter duration, gradually at prolonged and irregular intervals varying from 1 to 14 days, commonly 2 to 4 days. Previously two untreated cases had 8 to 10 relapses respectively.

Loss of appetite and constipation were common to all the cases. One case had epigastric discomfort, one nausea, one complained of pain in the eyes and one had arthritis of the knee. Cervical and epitrochlear lymph glands were enlarged in one case. Marks of tick bites were seen in 8 cases. Spleen was soft and enlarged in 4 cases, of these 3 complained of pain in the splenic region. Liver was palpable and tender in two cases, without any icterus. In Kashmir jaundice has been seen generally in those cases that assumed a low chronic form and remained untreated for over a month or more. One case had mild bronchitis; and one meningitis. Marked prostration and drowsiness were not present in

any case. Complications like iritis, pneumonia, hæmatemesis, epistaxis, delirium, herpes, nerve involvements did not appear and are not usual in the disease here. Similarly rash and secondary anaemia are not the features. Hæmaturia was seen previously, in one patient out of over 300 cases. There has been no mortality in 650 cases so far. The disease in Kashmir is milder than the louse-borne relapsing fever of India; and compared in severity with other tick-borne relapsing fevers, it appears to be more close to the Persian type than the Central African.

Laboratory Diagnosis

Parasites were seen in the blood of 15 cases, but were abundant in only a few. In one case whose blood slides were repeatedly negative parasites were seen after an injection of 0.5 cc. adrenaline. Two other cases failed to show spirochaetes in the blood, their diagnosis was confirmed by inoculating 1 to 2 cc. of the blood into white rats which showed parasites in the blood after an incubation period of 6 and 9 days.

Results of Streptomycin Therapy

The dose given to all the cases was one gram daily in two divided doses at 3 to 4 hours' interval for two consecutive days only. The treatment was started in 3 cases after the first paroxysm; in 3 after the first relapse; in 6 after the second; in 3 after the third; in one after the fifth; and in 2 after the sixth relapse. The last two had been previously treated with arsenic without any response. The results were equally good in all the cases.

The symptoms were markedly aggravated in some cases after the first injection. Headache and generalized aches became worse and the temperature rose. In 13 cases the treatment was started during fever and in 5 in the apyrexial interval. The symptoms were markedly aggravated in 4 cases after the first injection. Headache and generalized aches became worse, and in one the temperature suddenly rose from 99 to 103°F. In others there was only slight worsening of the general condition. After the second injection there was definite improvement in the symptoms; and when two grams had been completed the patients became asymptomatic within a week. The headache and aches disappeared, the appetite returned to normal and the bowels became regular. The liver and spleen, when enlarged, started regressing. None of the patients relapsed during an observation period of 1 to 2 months. No untoward symptoms due to the drug were observed.

Discussion

A trial with streptomycin on 18 cases of tick-borne relapsing fever of Kashmir has given . . . with a total dose of 2.0 g. only. The number of cases treated is not large enough to say that it can replace arsenic particularly as

the Kashmir strain of relapsing fever spirochæte, in vast majority of the cases, is not resistant to arsenic. Anti-syphilitic treatment of Indian troops with trivalent organic arsenical compounds caused a high incidence of arsenical encephalopathy. This fatal complication was noticed after the second or third injection specially in the Madrassies and the Maharattas. Poor nutrition and an attack of malaria played a significant rôle in its causation. Although up till now we have not encountered this complication in the treatment of cases of relapsing fever with arsenic, yet in view of our past experience with this chemotherapeutic agent during the last war, a safe substitute for reduction of this hazard will be of great help. Moreover, in the above series, two cases that did not respond to arsenic were cured with streptomycin. Therefore, the drug will have its definite usefulness for the treatment of arsenic resistant cases, or where arsenic is contra-indicated due to any reason.

Summary

Eighteen cases of tick-borne relapsing fever of Kashmir were treated successfully with streptomycin.

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MAN, A. (1947). 225, 769.

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ECHINOCOCCAL CYST OF BROAD LIGAMENT

By H. N. RAY, M.B., F.R.C.O.G. (Lond.)

Professor in Charge of Midwifery, National Medical Institute, and Senior Obstetrician and Gynaecologist, Chittaranjan Hospital

HYDATID disease of the broad ligament is a rare disease, and still more rare it must be when it is a case of primary infection. Only four such reports are available from the literature of recent years. Below are the interesting details of another case, and I have called it primary, because I did not find any lesion in the liver or elsewhere in the body nor was there a history of rupture of a cyst anywhere.

Case record

A married female, age 17, multipara, was admitted to hospital with the following complaints:—

1. Swelling of the lower abdomen for four months.
2. Slight pain in the lower abdomen, increasing during menstruation for 2 years.
3. Occasional retention of urine during last 2½ months.
4. Dyspareunia for about four months.

Onset.—For the past two years she had been suffering from a gargling sound in the abdomen with acidity, indigestion, anorexia and giddiness off and on. Nausea with alternate constipation and diarrhoea had been present during the last 3 to 4 years. In last July she felt definitely some heaviness in the lower abdomen and thereafter occasionally dysuria and retention of urine. She consulted some local doctor, and retention of urine was relieved by catheterization. On his advice she came and sought admission into the hospital.

Past illness.—She had suffered from kala-azar during childhood.

Family history.—Parents are enjoying good health though there is history of chronic anaemia in the family. No history of echinococcal infection either on the parental or husband's side. She was very fond of dogs and kept in close association with them.

Habits.—Besides looking after the dogs her daily work consisted in performing ordinary household duties and agricultural work. Menstruation normal but the flow was scanty and of serosanguineous type with offensive smell. There was intense dysmenorrhoea of the spasmodic type for the first two days.

Present condition.—General health below par, thinly built and slightly anaemic. Weight 78 lb. Secondary sex characteristics fairly developed. Liver and spleen not palpable nor tender. There was slight thickening and tenderness of the descending colon. A tense cystic swelling rather uniform and globular occupied the lower abdomen and extended nearly up to the umbilicus. It arose from the pelvic cavity, occupying the right iliac, hypogastric and a portion of the umbilical regions. The mass was slightly tender on palpation with limited mobility but free from the anterior abdominal wall. Percussion wave was present. Fœtal parts or movements were not felt.

P.V.—Cervix small in size with mobility restricted to the left. It was felt lying in front of a mass and slightly deviated to the left. A rounded, tense, elastic, cystic bulging could be felt in the posterior fornix, extending to the right side. There was no tenderness. This mass was continuous with the one felt externally. It occupied the pelvic cavity and pouch of Douglas and displaced the uterus to the left and slightly in front but was separate from it.

Blood.—Hb. 55 per cent, R.B.C. 3,970,000 and W.B.C. 6,800 per c.mm., poly 68 per cent,

lymphocytes 25 per cent, mono 4 per cent and eosinophile 3 per cent.

Blood sedimentation rate was normal. Coagulation time was 3 minutes 10 seconds. Obviously the patient was suffering from chronic anaemia of the hypochromic microcytic type which must have been due to the effect of the cyst as her blood picture quickly improved after its removal and the haemoglobin rose to 80 per cent in the short post-operative period.

Urine.—Normal. Kidney function test was also found to be normal.

Blood pressure.—I have found in a series of cases among Bengali women in this hospital, the normal blood pressure between 110 and 115 systolic and 65 to 80 diastolic. In this particular case it was found to be 130/90 which is rather on the high side. There was no history of rise of blood pressure in her family and this was verified by me in the case of individual members. The rise of blood pressure in this particular case might have been due to toxic absorption from the cyst. In fact, after removal of the cyst and when the patient regained her health from post-operative malady, the blood pressure came down to 110.

Operation.—Laparotomy was done on 31st July, 1948. A shiny mass, globular in appearance and cystic in feeling, was found arising from the pelvis. It grew between the layers of right broad ligament, displacing the uterus to the left and in front and the ovary to the right and posteriorly. Uterus, fallopian tube and ovary were free. There was no adhesion to adjacent structures. The mass had deeply burrowed down into pelvis and could not be lifted out. No blood vessel could be seen or felt as opposed to the observation on a case reported by James Oliver (*Lancet*, May 1912) where he mentions that 'It was well supplied with blood vessels which had to be tied and cysts were scraped out piecemeal'. The pelvic cavity was otherwise clean and there was no other secondary implantation. Taking proper precautions around the field for the prevention of surgical transplantation of the contents of the cyst, a small incision was made on the wall of the cyst, resulting immediately in expulsion of a small round cyst. The incision was then extended exposing a large number of cysts, which later on were counted and found to be about 300. They were picked out. Particular care at this stage was taken to avoid any cyst falling and disappearing in the pelvis. After opening the pericyst and removing the entire endo- and ectocyst, the cavity was cleansed and swabbed with tincture iodine. A good portion, i.e. about half of the whole sac (pericyst), was cut and removed. Then the margins were inverted and sutured together and the cavity was closed. Fallopian tube, ovary and uterus remained absolutely free. Beckwith Whitehouse in his book mentions troublesome hæmorrhage

but fortunately in this case bleeding or oozing of blood from the cyst wall was almost nil. Before closing the abdomen, the other structures specially the liver were examined and found to be normal. The post-operative condition of the patient was highly satisfactory. There was no reaction in the form of urticaria or high temperature due to toxin of hydatid cyst. The patient improved in health and was discharged in a short time.

Characters of the cyst.—Macroscopically cysts were spherical in shape and of different sizes, diameter varying from 1 mm. to 90 mm. The wall of the cyst was thin, soft, of gelatinous consistency, and translucent white in character resembling the white of half-boiled egg. They were present in a whitish opalescent fluid (figure 1, plate XIV). The cyst walls were readily coiled inwards when broken. There were brood capsules set free in the cystic fluid of the mother cyst. There were in addition a few pieces of fragmented thick-walled opaque white gelatinous membranous structures in roll formations suggesting wall of the mother cyst. Fluid was slightly alkaline in reaction, non-albuminous, had a specific gravity of 1.010 and contained chloride of sodium. The above cyst contained a thin transparent colourless fluid with a few crystals and a fairly large number of spherical and very thin-walled daughter cysts. These daughter cysts contained within a variable number of scolices which were mostly invaginated with crown of numerous hooklets and two pairs of suckers clearly seen (figures 2 and 3, plate XV). The infection is derived from food or water contaminated with faeces of dogs and occurs in men from close contact with them. The embryo which has six hooklets is freed from the egg by the digestive process and may reach any part of the body by burrowing through gut wall. Sixty per cent reach the liver by portal vein. After reaching the destination, the hooklets disappear and the growing embryo is converted into a cyst with an outer adventitious capsule, i.e. pericyst provided by the host and produced by the inflammatory reaction. The parasitic part of the cyst is composed of two layers, ectocyst and endocyst. The endocyst or germinal layer represents the most active tissue of the parasite: from it grow scolices bearing hooklets. From the parent cyst, daughter cyst and grand-daughter cysts are formed until a colony of cysts is produced.

The pathogenesis of hydatid disease of the pelvis has not been explained properly. Commonly it is believed that implantation in pelvis is due to transplantation from ruptured cyst of the liver. But the case that I have reported here seems to be a primary affection of the broad ligament. It is believed that the embryos after piercing the intestine reach the connective tissue beneath the peritoneum or they can be carried to this place by the blood or lymph. Affections of uterus, fallopian tube and ovary have also been reported.

Interaction between the host and parasite.—Three types of reactions are mentioned in the literature—(1) Immunity reaction: This provides a scientific test for the diagnosis of hydatid disease within certain limits. In this case this test was not done. (2) Leucoblastic reaction: There is as a rule increase of eosinophil leucocytes which is regarded as a strong presumptive evidence of hydatid invasion, but in this case, I am surprised, the count has never showed rise in eosinophils more than the average even on repeated examinations. (3) The toxic reaction: (a) Urticaria. (b) Local inflammatory processes from direct contact with hydatid fluid (peritonitis). Both (a) and (b) were absent in this case. (c) Chronic toxic effects, e.g. wasting and anaemia. These were prominent here. (d) Rise in blood pressure. This is not mentioned in the literature and is suggested by me.

Summary

1. A case of primary echinococcal cyst of broad ligament is reported.
2. Anaemia and rise of blood pressure were associated with the cyst.

PNEUMOPERITONEUM IN THE STUDY OF HEPATIC ABSCESS

By H. B. LAL

LIEUTENANT-COLONEL, I.A.M.C.

J. D. S. CAMERON and N. A. LAWLER have given aspiration with air replacement a place of very great importance in the treatment of liver abscess. Introduction of air into the abscess cavity was to assist in the study of the progress made by the latter in the process of healing, by radiological means. Although Cameron during his tenure as a physician consultant to AHQ(I) spared no efforts to popularize aspiration with air replacement as a method of treatment, it is felt that the medical profession has not taken to it with any great enthusiasm, there being certain objections to the procedure recommended by him:—

(a) It is not outside the experience of most physicians in the tropics that emetine in combination with organic compounds of arsenic and of iodine would resolve a very large proportion of hepatic abscesses, and that aspiration has to be resorted to only in exceptional cases in whom the abscess has reached a size when spontaneous absorption, after destruction of the amoebae and the secondary organisms, is not physically possible, or when an abscess originally amoebic has been converted into a pyogenic one by the secondary invader taking on a more prominent rôle.

(b) It has been demonstrated by McCallum that amoebae are found only in the margins of the living and not in the necrotic tissues of the abscess, unless the abscess has been opened to the air. He points out that this is because of their need for oxygen. An amoebic abscess presents very few amoebae even in the walls in a closed state, but their number greatly increases both in the walls and in the pus after being opened to the air. Air replacement after aspiration of the necrotic material can only give a further stimulus to the amoebae in the walls to increase in number and also to flourish in the remnant pus, and thus render the task of amoebicidal drug all the more difficult in dealing with them in the necrotic contents of the abscess cavity.

(c) Injection of air into a cavity, the volumetric size of which is not known, is not altogether free from risk. Injection of too great a volume of air might by increase in tension force the pus further into the healthy tissues or might cause a tear of the latter. Further, it is quite logical that absorption of air by inflamed abscess walls could not be efficient and the continued presence of air might delay the contraction of the cavity and its ultimate healing.

Cameron in common with most authors has recommended the site of election for aspiration to be the 8th to 10th interspace in the midaxillary line. But it is common experience that, more often than not, the abscess cavity proves to be very evasive, necessitating puncture of the liver in various directions before the pus can be struck, and then it cannot be definitely ascertained if the needle has entered the main abscess cavity or merely a subsidiary one.

To overcome all these difficulties, the author is anxious to introduce his method of the study of hepatic abscess by radiological examinations after induction of pneumoperitoneum. The author further feels that the treatment of every case of hepatic amoebiasis should be controlled by this method, whether the treatment is purely medical or aspiration has become necessary.

After insertion of air into the peritoneal cavity, an antero-posterior skiagram of the lower chest shows up the outline of the liver with great clarity along all its borders. The shadow of the superior margin of the liver becomes distinct from that of the diaphragm, separated by a narrow line of radiotranslucency between the two, with a break where the bare area of the liver is directly attached to the diaphragm. The lateral view shows up the break caused by the bare area even better. In the pathological lesions of the liver, study of the lateral views requires a clear knowledge of the appearances, as the picture is composite of both the halves of the diaphragm, and the variations from the normal have to be read mostly in relation to the shadow of the right half of the diaphragm.

The pathological appearances may take the following forms :—

1. Generalized enlargement of the liver, with a normal contour and a total absence of any adhesions, in cases of early hepatitis, with no definite tendency as yet of abscess formation.

2. Localized prominence of one or the other part of the contour without any adhesions to the diaphragm or abdominal wall in early precipitations of an abscess.

3. Localized prominence with neighbouring adhesions to the diaphragm or the abdominal wall, according to the situation, along with deformity of the diaphragmatic dome, in cases of definitely established hepatic abscess with a tendency to point in one direction or the other.

4. Generalized adhesions all round the liver resulting from a generalized hepatitis of a severe or prolonged type. This appearance is nearly always left with a persistent pain and tenderness in the hepatic area, with a slightly palpable liver, in spite of a most thorough treatment. This sequela can be explained either on the grounds of a partial passive congestion due to fibrotic constriction around the hepatic vein or due to a persistent low degree of hepatitis with cirrhotic tendencies.

5. Localized prominence of the lower surface of the liver in case the abscess is localized towards that surface.

6. Central abscess has to be concluded on clinical grounds, the presence of a more marked enlargement in one lobe, in the absence of any in the other.

It is within experience that the extent of the adhesions and their site are quite indicative of the ultimate prognosis of the case from the point of view of recovery from pain and tenderness in the hepatic area. Further, as the air in the peritoneum remains visible under the *x*-ray for about a week, the progress of the hepatitis or hepatic abscess can be watched in the early stages of the treatment on a screen.

The advantages of this method of serial study of hepatic amœbiasis lie in :—

1. Exact differentiation between a generalized hepatitis and a localized abscess, even at a very early stage of the latter.

2. Study of the progressive changes in the size and shape of the liver before, during and after the treatment, without in any way interfering with the pathological condition itself.

3. Exact localization of the hepatic abscess or localized hepatitis by study of an A.P. and a lateral view, its variations in size under treatment and the determination of the site where aspiration should be done if this becomes necessary.

4. Differentiation of hepatitis and hepatic abscess from other conditions of the liver, e.g. echinococcal cysts, new growths, etc. While

the former will retrogress under appropriate treatment, no such change will be seen in the latter.

5. Prevention of adhesions to the diaphragm and the abdominal walls, which contribute so much to the remnant pain and tenderness in the hepatic area.

6. Differentiation of the supra-diaphragmatic lesions from the sub-diaphragmatic ones—the best example is when the shadow of a collapsed lower or middle lobe of the right lung causes a continuous shadow with the liver. Pneumoperitoneum brings the diaphragm and the liver into contrast with that of the collapse. The presence of a long-standing inflammatory lesion at the base of the lung, however, produces adhesions on both sides of the diaphragm and may reduce the value of this method of differentiation.

7. Author's experience that pneumoperitoneum accelerates the recovery of the patient and contributes towards his well-being during the course of the treatment.

Certain objections have been raised to the induction of pneumoperitoneum in cases of hepatic abscess. The main fear has been one of tearing of adhesions around an abscess, already pointing either towards the diaphragm or the abdominal wall. Such an event has never materialized in the author's experience. Further, it may be pointed out that the introduction of 250–300 cc. of air into the abdominal cavity rendered the intra-abdominal pressure positive merely to the extent of +4 to +5 mm. of water, and this pressure is never enough to cause any separation of adhesions. A further precaution is taken, of schooling the patient to relax his abdomen, without which even the induction of pneumoperitoneum becomes difficult in the absence of a paralysed diaphragm, as any attempt at straining the abdominal muscles stop the flow of air. The question of infection of the peritoneum does not arise in the face of the safety with which the physicians have used this procedure in the treatment of pulmonary tuberculosis.

Technique

The patient usually requires no premedication. He is asked to evacuate his bladder; the lower abdomen is shaved and washed with soap and water, and cleaned with spirit. The part is then painted with acriflavine in spirit, covered with a sterilized towel till the operation is begun.

The pneumothorax apparatus is set with the water having been displaced to the distal bottle; and the air and manometer circuits completely closed against each other and the delivery tube.

The operation consists of primary induction of local anaesthesia at the midpoint between the pubis and the umbilicus. It must be stressed that the anaesthetic fluid must be injected with a small bore hypodermic needle and properly

infused under the skin into the underlying integuments and the peritoneum. After the local anaesthesia has taken effect, the pneumothorax needle is boldly inserted through the original puncture, till the peritoneal coat is pierced, when all resistance seems to give way. There is hardly any danger of puncturing or damaging the gut wall. The stylet is withdrawn and the needle connected to the delivery tube.

At this stage the patient is asked to relax the abdominal muscles completely. This is very important because any straining on the part of the patient will effect the manometric readings as well as the flow of air when the pneumoperitoneum is being induced.

Now the manometric circuit is opened to the delivery tube, and if the abdomen is well relaxed, a negative pressure of -2 to -4 will be registered, with slight variations with respiration. The manometric circuit is now completely closed and the air circuit opened to the delivery tube. The air will start flowing into the peritoneal cavity and can be heard hissing with the aid of a stethoscope and appearance of tympanic resonance in the abdomen. When 250 to 300 cc. have been injected, the circuit is closed and the needle withdrawn, the puncture wound being sealed with collodion.

The patient is then asked to sit upright for about ten minutes to enable the air to rise up below the diaphragm and around the liver and stomach. It is important that screen examination is done before the x-ray pictures are taken to determine the best views for the same.

The procedure could be repeated when re-examination is required.

For details of x-ray appearances see figures 1, 2 and 3 in plates XVI to XIX.

Summary

The idea of diagnosis, estimation and observation of the progress of amœbic hepatitis by serial skiagrams after induction of pneumoperitoneum is presented.

GENERALIZED CYSTICERCOSIS CELLULOSÆ

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CYSTICERCOSIS CELLULOSÆ is the term given to the somatic infestation of man by *Cysticercus cellulosæ*, the larval or bladder worm stage of tapeworm *Tenia solium*. Usually man is the definite host for the adult worm, being infested by eating measly pork; whereas in this condition he becomes the intermediate host for the embryos, the infestation occurring *via* food and drink contaminated from outside or from

lack of personal hygiene, - or - by reverse peristalsis, which helps in liberating the embryos in the upper part of the intestinal canal.

Cysticercosis cellulosæ cannot be considered a unique condition in man. It has been known since 1558 and several hundreds of cases were on record from Central Europe. During the first half of the nineteenth century it was seen in 2 per cent of autopsies in Berlin. This was at a time when uncooked ham was very popular in Germany. With improved hygienic conditions it became a rarity, so much so that a practitioner tended to forget it. Recent interest was revived by MacArthur (1934) who reported 22 cases of epilepsy in apparently healthy soldiers returning from India. Ten cases were due to cysticercosis. In another series of 82 cases of soldiers returning from India, 22 were proved to be due to cysticercosis. A number of cases was then reported by many other workers. The most notable reports are by Dixon and Hargreaves (1944) who have followed 284 cases of cysticercosis for ten years. Cases have been recorded from Mexico (Mazzotti, 1944), China (Ch'in, 1933; Chung and Lee, 1935), and other countries. In India there are very few recorded cases. The first record was an autopsy report by Armstrong (1888). From 1888 to 1947, there are about 12 reports, 7 being clinical cases and 5 autopsies, one case only being followed both clinically and by autopsy examination. The first clinical report was by Williams (1906), a case of cysticercosis of the tongue. Second was by Elliot and Ingram in 1911, a case of sub-conjunctival cysticercosis and another similar case by Wright in 1923. The fourth case was recorded in 1935 by Dogra and Ahern, a case of cysticercosis in a British soldier residing in India. Fifth and sixth cases were of somatic taeniasis reported by McRobert in 1944 and Subramaniam in 1946. The seventh and the last known recorded case was a case of cysticercosis resembling myopathy by McGill in 1947. The first autopsy record is by Armstrong in 1888, second by Williams in 1906, third by Tirumurti in 1911, fourth by Krishnaswami (1912) and fifth by Campbell and Thomson in 1912, the last being the case that was followed clinically and by autopsy examination.

Most of the above recorded cases in India are from Madras and South India, while those reported in Dixon and Hargreaves' (1944) series were from the Punjab and the United Provinces. Cases of cysticercosis are rare in Bombay. It may be added here that Dr. P. V. Gharpure, Professor of Pathology of this institution, came across a case of cysticercosis in 1947; the case had been referred to by the Tata Memorial Hospital, Bombay. Recently an autopsy case of generalized cysticercosis cellulosæ was encountered in Bombay again, which supplies the first autopsy record of its kind here. A brief report of this case is given below :

Autopsy Report

Clinical notes.—The patient, a Hindu male, aged about 30 years, was brought by the police from the roadside in a drowsy condition. Clinical examination: Neck rigidity, rise of temperature, Kernig's sign were absent, the normal plantar response was obtained. C.S.F. was under tension and clear, urine was normal. Blood count: Total W.B.C. 6,200, polymorphs 62 per cent, lymphocytes 30 per cent, eosinophiles 6 per cent and monocytes 2 per cent. Patient died after 30 hours in the hospital.

External examination.—The body was that of a male, aged about 30 years, fairly well-built but poorly nourished. Pupils were normal. Four to six cystic nodules were palpable in each side, on the side of the neck and upper part of arms.

General examination after opening the body.—Numerous cysts were seen in the subcutaneous tissue of the thoracic wall and abdominal wall over and above the nodules palpated on the surface. The cysts were on an average 1 cm. \times 1 cm. in size and loosely attached to the surrounding tissue, and could be easily separated for examination.

Examination of viscera.—Heart: Two cysts were seen on the anterior aspect and one big cyst posteriorly at the base, near the origin of big vessels, with some smaller less conspicuous cysts. All were attached loosely. Heart was normal in size, and valves and chambers did not show any abnormality. Coronaries and aorta were normal.

Lungs: Two big cysts, size about 1.25 cm. \times 1.5 cm., and several other smaller cysts were seen in the lung substance at the apex of the right lung. Both the lungs showed marked congestion.

Diaphragm: Numerous cysts were attached to the diaphragm on either side.

Brain: Meninges were normal. Numerous cysts were seen in the brain tissue by external examination and section examination, which showed the cyst being present in the wall of the ventricles also.

Tongue, pharynx, larynx, trachea, œsophagus, stomach, intestines, rectum, bladder, prostate, testes, ureters and adrenals were all normal.

Spleen and liver were enlarged and darkly pigmented by malarial pigment.

The skull bones were normal, the long bones were not examined.

The adult worm was not seen in the intestinal tract. There were no parasites of any kind in the intestinal tract.

Examination of cyst: Size 1 cm. \times 1 cm., transparent with a milky spot inside. On cutting open the wall slightly turbid fluid escaped. Examination of scolex showed suckers and hooks typical of *Tania solium*.

Histological examination.—Brain: The cyst was surrounded by a wall of neuroglial tissue.

Moderate amount of mononuclear infiltration was seen.

Heart: Surrounding structure showed fibroblastic reaction and mononuclear infiltration.

Lungs: Showed passive congestion.

Liver and spleen: Showed malarial pigment.

Photographic records.—The cysts are seen in the photographs of brain section, heart, lung and portion of thoracic wall (figures 1 to 5, plate XX).

Discussion

1. The maximum number of cysts was found in the brain tissue. This is in accord with the fact that the embryos of *Tania solium* show special predilection for the nervous tissue. This tendency in the living state of the patient gives rise to several important clinical states, viz. epilepsy, other psychoneurotic states, blindness and other ocular manifestations. The above findings coupled with palpable nodules in most of the cases, though not in all, give an important clue to the clinical diagnosis of this condition. In some cases where the nodules are not found, surgical exploration of brain for diagnosis is helpful, though this is rarely required in practice (Dixon and Hargreaves, 1944).

2. Unfortunately in this case the patient came in in an extreme state and therefore it was not possible to decide whether it was an imported case or got infested locally. Neither was an account of clinical symptoms available. It might be expected that some general reaction on the part of the host would occur at the time of a heavy infestation of the tissues with the embryos, giving rise to illness of a vague nature. Those who have followed such cases have frequently observed this initial vague illness with the variety of symptoms. Some of the cases, which proved to be of cysticercosis afterwards, were found to have been entered on medical history sheets as cases of sandfly fever, headache, myalgia, P.U.O., 'clinical malaria', and transient rashes suggesting allergic manifestations (Dixon and Hargreaves, 1944).

3. None of the cysts was calcified. All cysts were loosely attached to surrounding tissues. This is the condition found during the earlier stages of the disease, there being little reaction by host tissue. When the embryos die, foreign body reaction starts ultimately resulting in calcification. Hence excision of a cyst and examination under the microscope is possible for diagnosis in early stage. Radiological examinations are of value only after calcification has occurred.

4. The adult worm was not found in the intestine. This is not an unusual finding. An important mode of infection is contamination of food and water by those harbouring the worm, helped by the agency of flies. Hence stool examination may not be of help in all cases. The possibility of this condition in non-pork eaters also cannot be ruled out.

5. Blood examination did not show eosinophilia. Eosinophilia is not very common in infestation with *T. solium*. Thus it is not of much help in the diagnosis of this condition.

6. The C.S.F. was under tension and clear. Routine C.S.F. examination does not help in the diagnosis. The increased tension indicating increased intracranial pressure is an observation found in many cases with cerebral infestation. This may cause papilloedema and blindness, an acute condition which can be relieved by decompression, a procedure of much value in saving the sight of the patient.

7. MacArthur's cases and those reported by Dixon and Hargreaves are of special significance. The soldiers in their series were mostly those who had been in India for some time and had got infected in India.

Those investigating the causes of epilepsy and many other psychoneurotic states and blindness in this country should not forget cysticercosis as a possible cause. The suggestion is not a novel one as it was suggested as far back as in 1936 in the editorial of *Indian Medical Gazette*.

Report of a clinical case in 1947 and an autopsy record now are a sufficient proof to show that the condition is prevailing in this country.

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SOME CONSTITUENTS IN NORMAL BLOOD IN CENTRAL INDIA

SERUM PROTEINS, SERUM ALBUMIN, SERUM GLOBULIN AND SERUM NON-PROTEIN NITROGEN

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In modern medical practice, one occasionally requires the albumin-globulin ratio on a patient's

serum in order to arrive at a correct clinical diagnosis in certain types of cases. The standard normal values referred to in such cases are those from western standards. No such standard normal values exist for Central India people in particular though Bose, De and Mukerjee (1946) have published a normal standard for Indians. The need for such work was felt more keenly on account of changes in the diets of different provinces in India and westerners.

The methods used for these estimations are partly physical and partly chemical. The striking physical peculiarities of the serum proteins and the fact that they constitute a greater part of the serum solids, make this an inviting problem—a problem of finding conditions under which one easily determined physical constants of serum could be used as a measure of the protein contents. Starlinger Hartl (1925) have reviewed methods based on interferometric, polarimetric, viscosimetric and refractometric measurements, all of which are influenced by the protein contents among the serum constituents. Of these only the refractometric measurements have been of practical value in general clinical work. They have been used not only for total protein estimations but also for the albumin and globulin fractions separately (Neuhausen and Rioch, 1923; Robertson, 1915).

Of the physical methods, the specific gravity determinations of the serum have proved to parallel the protein contents closely enough so that the specific gravity determinations are of practical use in clinical studies. This property has been already made use of by us in one of our previous works on the determination of total proteins in plasma (Gokhale and Lokre, 1947).

The chemical method may be classified into three categories by the following processes:

(1) Coagulating the proteins and then weighing the coagulum,

(2) redissolving the proteins and then estimating them quantitatively by using one of the protein colour reactions and

(3) determining the nitrogen contents by digestion methods.

In order to suit ordinary laboratory conditions and also to minimize the extra labour for using a separate method for the determination of the non-protein contents, we fell back on the last of the chemical methods for our work. Serum, free from haemoglobin, was used for the purpose. The donors were chosen from amongst the members of the staff and students of the King Edward Hospital and Medical School, Indore. These were young, apparently healthy persons between the ages of 20 and 36 years, naturalized for the Central India climate and food conditions. Fasting blood samples of these were collected by means of a dry

sterilized syringe. The clear serum was used for the purpose of the various estimations. The details of the technique used are given below (Stitt *et al.*, 1948).

Total proteins.—Into a 50 cc. volumetric flask, pipette 1 cc. serum and dilute to the mark with 0.9 per cent of saline (sodium chloride). Mix well. Transfer 1 cc. of the diluted serum into a pyrex digestion tube, 200 × 32 mm.

Albumin.—All procedures were carried at incubator temperature 37°C. To 1 cc. serum in a 50 cc. flask, add 33 cc. of a 22.2 per cent solution of anhydrous sodium sulphate, mix and incubate exactly for 3 hours. After this filter repeatedly till a water clear solution is obtained. Transfer 1 cc. of this filtrate to another similar pyrex tube. The sodium salt is used to separate the globulin.

The process of digestion is common to both the estimations.

To both the tubes add 1 cc. of 50 per cent sulphuric acid (nitrogen-free) and a few chips of porcelain. By means of a spirit lamp flame of which has been adjusted to a height of $\frac{1}{2}$ inch, heat for about 10 minutes. In this period most of the water vapours will be given out and dense white fumes will start escaping. When the dense white fumes come out, cover the mouth of the tube with a watch glass and continue

heating for 20 minutes. In this period the solution becomes dark, dense white fumes escape and the solution may or may NOT become clear. Cool for 1 minute, add 0.5 cc. of a saturated potassium persulphate solution, replace the watch glass and continue heating for 5 minutes, and cool for one minute. The solution will now be usually clear. Add 0.5 cc. of persulphate solution, replace the watch glass and heat for further five minutes. The contents of the tube must be clear now. If not clear, heat further for 5 minutes. Allow to cool.

Take two tubes graduated at 35 and 50 cc. and mark them Tp and Ta and transfer the contents of the tubes by washing with distilled water, that for the total proteins to Tp and that for albumin to Ta. Dilute the contents of the tubes to 35 cc. mark with distilled water. If necessary, these should be filtered through a filter paper.

In another 50 cc. volumetric flask, put 30 cc. of distilled water followed by 3 cc. of standard ammonium sulphate solution containing 0.15 mg. of nitrogen, 1 cc. of 50 per cent sulphuric acid and 1 cc. of potassium persulphate solution. Simultaneously nesslerize with 15 cc. of the Nessler's solution, the standard flask and the unknown tube Tp and Ta. Compare the colours. A few drops of 2 per cent gum ghatti solution was added to all the tubes to avoid

TABLE

Serial number	Age	Diet	N.P.N.	Total proteins	Albumin	Globulin	Albumin/Globulin
1	36	Veg.	30.00	6.920	4.330	2.590	1.669
2	22	Mix.	30.00	6.401	4.493	1.908	2.354
3	22	Mix.	24.00	6.637	4.687	1.950	2.413
4	23	Mix.	30.00	6.412	4.493	1.919	2.237
5	24	Mix.	30.00	6.324	4.417	1.907	2.316
6	23	Veg.	24.00	6.637	4.532	2.105	2.153
7	24	Mix.	23.00	7.106	4.250	2.856	1.488
8	24	Mix.	22.90	7.285	4.178	3.107	1.311
9	20	Veg.	29.70	6.601	3.950	2.651	1.490
10	26	Mix.	30.60	6.500	4.019	2.481	1.620
11	24	Mix.	33.33	6.716	3.663	3.048	1.200
12	21	Mix.	31.50	6.418	3.649	2.769	1.310
13	24	Mix.	30.00	7.125	3.959	3.166	1.250
14	26	Veg.	31.90	7.018	4.013	3.005	1.230
15	25	Veg.	33.33	6.955	3.821	3.134	1.230
16	23	Veg.	33.33	7.006	4.063	3.043	1.330
17	25	Mix.	25.00	7.291	3.981	3.310	1.200
18	28	Mix.	32.90	7.125	4.125	3.000	1.370
19	21	Mix.	30.00	6.281	3.939	2.342	1.670
20	22	Mix.	33.33	6.477	4.063	2.414	1.680
21	22	Veg.	28.50	7.208	4.025	3.233	1.240
22	24	Mix.	40.00	7.645	4.157	3.488	1.190
23	23	Mix.	30.00	7.130	4.984	2.148	2.320
24	24	Mix.	31.40	7.302	4.639	3.366	1.270
25	23	Mix.	34.90	7.108	4.833	2.275	2.120
AVERAGES			30.156	6.865	4.210	2.688	1.626

Mix. = Mixed diet. Veg. = Vegetarian diet.

Figures for N.P.N. are in mg. per 100 cc.

Figures for total proteins and for albumin and globulin are in gm. per 100 cc.

precipitation. Hellige's bio-colorimeter is used for matching the colour.

Non-protein nitrogen.—This was separately determined in each case by Folin and Wu method using phosphoric-sulphuric acid-copper sulphate digestion mixture (Kolmer and Boerner, 1945).

The globulin.—The globulin content is obtained by subtracting the albumin value from the total proteins so obtained and the albumin-globulin ratio is calculated therefrom.

For calculating the total proteins and albumin, the following formula is used :—

$$\text{Protein \%} = \left\{ \frac{\text{Standard} \times 0.15 \times 100}{\text{Unknown} \times V} - \text{N.P.N.} \right\} \times \frac{6.25}{1,000}$$

where V is the volume of serum. The value for

V for proteins is 0.02, and

V for albumin is 0.0323.

The table above gives the values recorded and the averages arrived at.

Reagents

1. Fifty per cent sulphuric acid—A 50 per cent by volume dilution is used.

2. Saturated persulphate solution—Put 6 to 7 gm. of potassium persulphate (nitrogen-free) in a bottle and add about 100 cc. of distilled water. To ensure saturation, some undissolved crystals should remain. It is advisable to renew this every few weeks.

3. Saturated sodium sulphate—Dissolve 22.2 gm. of anhydrous sodium sulphate in about 80 cc. of water by the aid of heat. Rinse into a 100 cc. volumetric flask and dilute to mark with water.

4. The other reagents are those used in non-protein nitrogen determinations as per Folin and Wu's method.

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CREEPING MYIASIS IN MAN

AN UNUSUAL CASE

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MYIASIS is the condition or conditions resulting from the invasion of the tissues and organs of man and other animals by the eggs or larvæ of dipterous flies. Such invasion may be simple, i.e. without any severe constitutional disturbances, or may result in violent disturbances causing even death. According to the site of invasion one may have cutaneous, dermal, intestinal, urinary, nasal, oral and auricular myiasis.

There are various myiasis producing Dipteras and according to the ovipositing habits of the females they are classified into (a) specific myiasis producing Diptera, (b) semi-specific myiasis producing Diptera, and (c) accidental myiasis producing Diptera (Patton, 1921).

Specific myiasis producing Diptera.—The larvæ of the flies of this group are found only in living tissues. The flies generally select a number of tissues or organs or one particular organ in which or near which to lay their eggs or deposit their larvæ. These are (a) *Chrysomya bezziana* causing a massive infestation and the tissues rapidly break and suppurate. This is a specific myiasis producing fly of India, Burma and Ceylon. (b) *Cordylobia anthropophaga* and *C. rodhaini*. The larvæ of these flies are subdermal migratory forms and live beneath the skin and subcutaneous tissues of man and animal during greater part of their life. Generally, one larva causes myiasis and no great tissue destruction and suppuration occur. (c) *Wohlfahrtia magnifica*. This fly deposits its larvæ in cuts, sores, wounds and at the entrance of nostrils and vagina and on the eyelids, the fly being attracted by an offensive discharge from such tissues or organs. (d) Flies of the family Oestridæ. In this family are included large number of highly specialized flies whose larvæ can reach the maturity in certain tissues and organs of special animals and their near allies. The larvæ are found for the most part in three locations of their hosts, the stomach, the nasal passage and the skin. Usually they are found in wild and domestic animals and only occasionally and accidentally in man (Young, 1944). The entire larval stage of the Oestridæ is a long one, and is chiefly passed in the third stage. The adults are short-lived. Oestridæ other than *Hypoderma* and *Dermatobia* do not infect humans. Even in the case of these latter flies the larvæ have not so far been found to reach the third stage of their life cycle (Smith and Greaves, 1946). The flies of the family Oestridæ responsible for myiasis are: *Æstrus ovis*, *Hypoderma bovis*, *H. crossi*, *Gasterophilus hæmorrhoidalis*, *G. nasalis*, *G. intestinalis* and *Dermatobia hominis*.

Semi-specific myiasis producing Diptera.—The flies of this group breed normally in the bodies of dead animals, decaying vegetable matters and excrements. They may occasionally lay their eggs or deposit their larvæ in the diseased tissues of man and animals, the female fly being attracted in each case by foul discharge from the sore, wound or diseased organs. The flies of this group are: *Calliphora*, *Cochliomyia*, *Pollenia*, *Phormia*, *Lucilia*, *Sarcophaga* and *Apiocnata*.

Accidental myiasis producing Diptera.—These flies normally breed outside the human body in organic and vegetable matter and when accidentally taken by man in his food may cause intestinal myiasis. There is no reason to believe that these flies intentionally deposit their eggs or larvæ on human food in order to reach the intestines; the food is merely used as a breeding ground. The flies of this group are: *Sarcophaga*, *Fannia*, *Drosophila*, *Anthonomyia* and the rat-tailed larva of *Eristalis*.

Mention must also be made of some blood-sucking larvæ belonging to the family *Calliphoridae*. Though strictly speaking they do not produce myiasis, yet should be included here as they produce wounds, generally on the foot, from where they suck blood at night and produce ulcers by the consequent secondary infection. They are larvæ of *Anchmeromyia luteola*, the 'Congo floor maggots' found on the floor of the native huts in Africa.

Report of the Case

The patient, a young man of 24 years, of average but muscular build and an inhabitant of Bengal, suddenly found a tumour-like swelling on the right thigh one morning with slight pain in it, about three weeks after he had returned from a tour in Delhi and suburbs. There was no tenderness or pain in the adjacent areas. This tumour moved towards the knee joint next day and left no pain or tenderness in its original site. From the third day onwards it started travelling back towards the right buttock and subsequently towards the right side of the back, right shoulder and right eyebrow. This whole course took about 15 days and left no mark in those places where the tumour was visible during its travel. The right eyebrow and the adjacent areas were considerably swollen with accompanying pain. There was no fever or any other constitutional disturbances. Blood examination showed very slight rise in eosinophil count: W.B.C. 8,550, poly 60 per cent, lympho 25 per cent, mono 5 per cent and cosino 10 per cent.

The patient was treated outside with various drugs but without any effect. The pain and inflammation used to subside and come again. After about a week's treatment a red pimple about the size of a mole appeared on the tumour with a small pin-point black spot in its centre.

This was opened by means of a sterile needle and the contents of the tumour were expressed. A living maggot about $\frac{1}{2}$ inch long came out with a small amount of serosanguineous discharge. The maggot was preserved in spirit for identification and hot boric compress was applied on the tumour which subsided completely within three days without any complication. The patient was kept under observation for ten days within which no other tumour appeared on any other part of his body. This patient usually enjoys good health and plays games regularly. He is in the habit of sitting on the grass and take rest after the game is over.

Identification of the Maggot

Maggots, the larvæ of flies, are footless, whitish, creamy or brownish in colour and segmented. They taper anteriorly and are blunt posteriorly. Ordinarily there are ten to twelve visible segments. Full-grown larvæ greatly differ in size and length in different species of flies. The main diagnostic features, are the posterior spiracles or breathing apparatus situated at the blunt end, the cephalopharyngeal skeleton situated anteriorly at the tapering end and the anterior spiracles situated antero-laterally on the second segment. The last feature however can be distinguished only in a full-grown larva. The most distinguishing feature is the posterior spiracles whose size and shape, the distance between the plates, presence or absence of the button and general structure of the slits are different in different species of fly larva. This is examined by cutting from the posterior end of the larva a thin slice which is treated with caustic potash and mounted in canada balsam.

The present larva was $\frac{1}{2}$ inch long with ten visible segments, brownish white in colour with irregular rows of spines on the segments but without any bristle or hair on the body. The mouth parts and the posterior spiracles were dissected out, cleared and mounted. The anterior spiracles were not visible. It was seen that the oral hooks were bifid at their distal end, the proximal ends were blunt and a median chitinous process projected between them. The posterior spiracles were composed of varying number of rings, about thirty in number, more or less bound together in a black mass. From these features the larva was identified as the larva of *Hypoderma bovis* De Geer. It was in its second stage of life cycle as the development was not complete.

Life history of *Hypoderma bovis*

Hypoderma bovis is the warble fly whose larvæ are usually found under the skin of cattle where they cause swelling or subcutaneous tumours known as 'warbles'. No less than 50 per cent of the hides exported from India are damaged owing to the holes caused by these

larvæ. The adult fly is active in hot sunny days and darts at the animals with much buzzing and clings to the skin for a second while ovipositing one egg at a time. The egg is at once glued fast to the base of the hair close to the skin. The fly then retreats and strikes again after a few minutes for ovipositing again. Egg laying does not cause any irritation to the animal. A dozen or more eggs may be attached to a single hair which looks like a comb. Within 3 to 4 days or utmost a week small larvæ hatch out and try to burrow into the skin, which causes great irritation to the animal and the animal starts licking the parts. This way the larvæ are carried to the œsophagus and stomach of the animal. In course of months these larvæ gradually work their way through the muscle and finally lodge themselves on the back under the skin causing tumours or 'warbles'. Here they pass their third stage. Before pupation they come out from the tumours through a fine hole which is always there as a pimple and through which the larvæ breathe. Generally, there is one larva in a tumour. They moult for the last time and fall on the ground and burrow the earth to pupate there. The adult flies emerge from these burrows on the ground.

The life history, however, is very incompletely known due to the difficulty of observing the stages in the living animals. It seems that *Hypoderma* is confined to Western India from the Punjab southwards probably as far as Gujrat. It is not found in Bengal proper; only to a small extent in hilly countries (Lefroy, 1909). The first stage larva occasionally attacks man when he comes in contact with the infested cattle or possibly the grass on which the larva has fallen during the course of the animal licking its skin. (The patient is in the habit of sitting on the grass for rest after a game.)

Discussion

The mode of infestation in this case is not known. Most probably the egg or first stage larva became attached to the patient's clothes or skin while he went out on tour to Delhi and adjacent areas. Slight irritation due to burrowing of the skin passed unnoticed. The fact that the larva was expressed without pain or discomfort at an immature stage showed that it does not complete its life cycle in the human host. It is doubtful whether the treatment administered precipitated the appearance of the tumour in the upper eyelids. The migration is said to be maintained to avoid encystment of the larva. There is, however, every possibility of other larvæ being present in this case though no sign or appearance of any other tumour has been observed.

Summary

A rare case of human myiasis due to warble fly larva is reported. A short description of

myiasis producing Diptera is given. The larva recovered has been identified as the larva of *Hypoderma bovis* in its second stage of life cycle. Contact with infested cattle or resting on infested ground was probably the mode of infection. No special treatment was necessary.

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EPIDEMIC DROPSY COMPLICATING PREGNANCY

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IN Bengal cedema of legs is one of the commonest complications during pregnancy especially from the 6th month onwards. It is so common that if the cedema be slight, elderly ladies rarely think it unnatural. From clinical experience it is the opinion of every practitioner that the incidence of these cases has increased in number since 1944, i.e. after the great famine of Bengal of 1943. During this year the number has increased further. Generally in these cases pregnancy ends prematurely in the 8th or 9th month. Sometimes foetuses die in the uterus and macerated babies are delivered within a few days after death. In another group still-born babies are delivered. In a third group babies delivered alive die within one to two months after birth. Therefore, foetal mortality is high. Generally, the babies are small in size, i.e. in length and weight. Nowadays the average weight of babies delivered in hospital is below 6 lb. If other conditions are normal delivery is not prolonged and occurs without any external aid. There is postpartum hæmorrhage in some cases. During puerperium there is danger of sepsis because the vitality of the patient is low in these cases. Therefore, strict aseptic precautions should be taken during delivery. If there be any suspicion of sepsis penicillin should be administered prophylactically.

Common causes of cedema of legs during pregnancy are :—

- (1) Anæmia (hypoprotinæmia). (2) Pre-eclamptic toxæmia. (3) Chronic nephritis. (4) Essential hypertension. (5) Heart disease. (6) Epidemic dropsy.

Due to scarcity of diet anæmia during pregnancy is very common. This is clinically

verified by blood examination and blood pressure report. Generally, the red blood cells vary from 2.5 to 3.5 million and hæmoglobin from 50 to 70 per cent even in so-called normal cases. In hospital and private practice cases below this level are found in greater number than before. In Bengal systolic pressure in women varies from 95 to 110 mm. and diastolic from 60 to 80 mm. In uncomplicated anaemia generally the blood pressure is low (in anaemia due to chronic nephritis blood pressure, both systolic and diastolic, is high). Urine examination sometimes reveals slight albumen. Since 1944 (i.e. after the Great Bengal Famine of 1943), large number of cases of pregnancy with R.B.C. below 2 millions and hæmoglobin below 40 per cent with diarrhoea in some cases are found. As groups 2 to 5 are mentioned in detail in every book, it is needless to mention them.

Group 6.—Of late we are coming across another group of cases where slight œdema of legs begins from the 1st or 2nd half of pregnancy. Patients generally complain of palpitation on slight exertion and some complain of disturbances of vision. Pulse rate is more than normal. In some cases the heart is found to be dilated. After enquiry it is found out that most of the members of the family (both male and female) are suffering from the same complaints. This year these cases are not rare. (Routine examination should be done—i.e. general examination—examination of B.P., urine, blood, fundus of the eye, if necessary, electro-cardiogram.)

Only 13 cases of this group, from private practice, are mentioned below :—

The cases were examined for the first time in the 7th, 8th and 9th month of pregnancy with the symptoms of slight œdema of legs, palpitation of heart and general weakness. Dimness of vision occurred in 3 cases. In 2 cases there were the additional symptoms of non-movement of the fetus. General examination revealed œdema of both legs, slight dilatation of the heart in some cases and increased pulse rate. In all the cases blood pressure was recorded : systolic pressure was 110 or below in all the cases excepting one in whom it varied from 120 to 130 mm. (aged 32, vi gravida). But the diastolic pressure was low almost in all the cases. In all the cases urine was examined but in only one was a trace of albumen detected (aged 32, vi gravida). In all cases blood was examined, percentage of hæmoglobin varied from 60 to 70 per cent and the number of R.B.C. from 3 to 3.5 million per c.mm. Pulse rate in all was below 100 in resting position. These cases were diagnosed epidemic dropsy with pregnancy, clinically.

Out of 13 no foetal movement was detected in 2, nor were foetal heart sounds heard, therefore, diagnosis of foetal death was made. Within 2 to 3 days macerated babies were delivered without any external aid, one in the 8th month, another in the 9th month of pregnancy. Another 2

were delivered of still-born babies in the 9th month of pregnancy within a week after the first examination. Delivery was normal and the W.R. negative in the above 4 cases.

The remaining 9 were delivered of living babies; out of these 2 died within one month. These 2 were delivered within a fortnight after the examination. The remaining 7 patients were treated for more than a month before delivery. In all the above cases there was no history of œdema of legs in previous pregnancy or delivery of any macerated or dead babies previously. (Edema was first detected from 5th to 7th month of pregnancy.

Rh factor and estimation of protein could not be done due to prohibitive cost, as all the cases came in my private practice from middle-class family.

Fœtal mortality—46 per cent (out of 13, 6 dead).

Treatment.—Glucose 25 per cent 25 cc., 'Berin' 100 mg. and choline 100 mg. intravenously in the morning—rest. Granule calcium gluconate one teaspoonful twice daily morning and afternoon. Multivitamin tablets BD, plastules with liver extract, BDPC elixir and vitamin B complex 2 teaspoonfuls twice or thrice daily.

Diet.—Milk, vegetables, fruits, bread, butter, fish, etc. Rice and mustard oil were absolutely stopped.

Generally, the patients improve and fœtal mortality is less if the treatment is commenced early. The treatment should be continued even after delivery—duration depending on the condition of the patients.

During pregnancy if the women get balanced diet, specially fish $\frac{1}{2}$ to 1 *poa* and pure milk one seer daily (1 *poa* 4 times a day) and get the advantage of antenatal clinic, can save themselves from over exertion—proper rest of about 2 to 3 hours at midday and 8 hours in the night—the number of these cases will surely decrease and fœtal mortality will be low.

TYPHUS IN MYLLIEM STATE AREA, SHILLONG

By I. B. ROY, L.M.P., D.T.M.

THE incidence of typhus in the surrounding hill tracts of Shillong in an endemic form is an occurrence more than one year old. It might have been present for a far longer period, but the presence of the disease was seldom suspected. In this series the first case that was positively diagnosed by a high titre Weil-Felix reaction occurred on 27th November, 1948. After that many more clinically typical cases have come under observation, ages of the patients being between $2\frac{1}{2}$ to 56 years, but blood could not be

differentiated keratinizing squamous carcinoma (figure 2, plate XXI). The epidermis in the pigmented patches showed an increase of melanin pigment which was found not only in the basal cell layer but also in many of the cells of the stratum spinosum. There was a moderate degree of hyperkeratosis. The sub-papillary layer of the dermis was acellular excepting for groups of melanophores scattered here and there. The elastic fibres in the deeper parts of the corium appeared markedly swollen and were aggregated into bundles (figure 3, plate XXI), an appearance resembling the one described by McCarthy (1931).

Treatment

The growth was fulgurated on 1st June, 1949, and a course of deep ray treatment was commenced on 13th July, 1949. The tumour regressed rapidly leaving an ulcerated area at its original site (figure 1, plate XXI). Local oily applications to the skin, combined with general tonics and administration of vitamin B and C, caused no change whatever in the skin condition.

Comment

This case presents features which are typical of xeroderma pigmentosa. In the first place, the patient was the offspring of a consanguineous marriage, his parents being first cousins. Macklin (1936) in his critical analysis gives statistical evidence to show the important rôle that consanguineous matings play in the causation of the disease. Secondly, the clinical features of this case, viz, the initial photophobia, characteristic pigmentation and the onset of carcinoma at an early age, in the absence of exposure to arsenic or x-rays, agree in all respects with previous descriptions of the disease (Sutton, 1939).

The histology of the skin also lends support to the diagnosis. However, the absence of the disease in any of his brothers and sisters would at first sight appear to make this diagnosis less probable. Several reports indicate that the disease has affected more than one member in the same family (Corson and Knowles, 1928; Bell and Rothnem, 1937; Loewenthal and Trowell, *loc. cit.*).

However, the only unusual feature, viz, the absence of the disease in other members of his family, has not deterred us from making this diagnosis. Macklin (*loc. cit.*) in his exhaustive review states that, because of the average small size of families, more families with one child than those with more than one are affected. The death of four out of seven children at the early age of 2 years has probably made our case fall into the category of Macklin's small-sized family with only one child affected with the disease.

Summary

1. References have been made to the few cases of xeroderma pigmentosa reported in

India, and a case in a Sinhalese is reported from Ceylon with a brief description of the histological features.

2. The case presented all the features of the disease excepting that only one member of the family was affected. This point has been briefly discussed.

Our thanks are due to Dr. A. S. Rajasingham, Visiting Surgeon, General Hospital, Colombo, for permission to report this case, Professor Govinda Reddi, Professor of Pathology, Madras Medical College, for his information regarding the Indian cases, and Mr. K. M. M. Michael of the Department of Pathology, University of Ceylon, for the photographs.

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EFFECT OF FIBROLYSIN AND ANTI-THYROIDIN ON RAYNAUD'S DISEASE (AFTER SYMPATHECTOMY)

By S. K. DATTA, B.Sc., M.B.

and

P. C. THAKURTA

A BENGALI Hindu male, aged 45, was suffering from acute intermittent pain in his left leg, specially in the afternoon, nearly for a year. He consulted some local physicians but got no relief. In 1948, in its early part, the pain became more acute and parts round ankle joint became swollen, and he secured admission in the Lake Medical College Hospital, where he was treated for four months, for the last three months of which the limb was in plaster.

This aggravated his condition. The foot and lower part of the leg became discoloured, and ulceration started in the great and middle toes. He was discharged. The pain now required morphia, once or twice daily in the afternoon and the dose gradually had to be raised from $\frac{1}{4}$ to $\frac{1}{2}$ grain.

PLATE XIV

ECHINOCOCCAL CYST OF BROAD LIGAMENT : H. N. RAY. (O. A.) PAGE 88

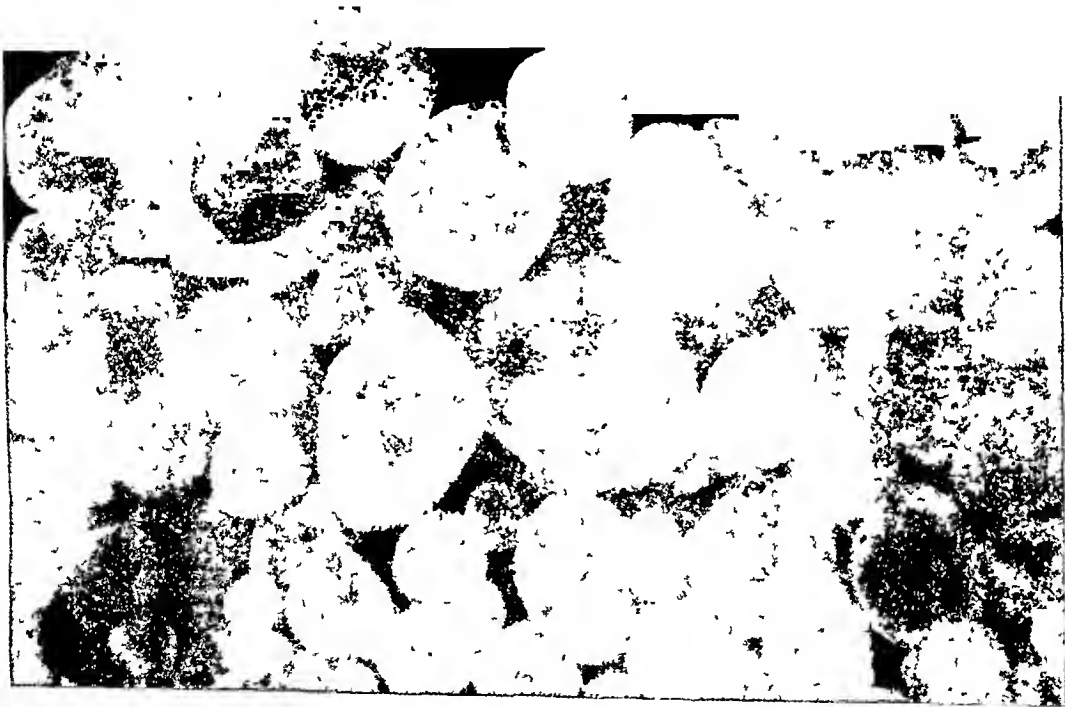


Fig. 1.



Fig. 2.



Fig. 3.



Fig. 1.—Large hepatic abscess—with adhesions to lateral chest wall.
(a) Normal A.P. view.

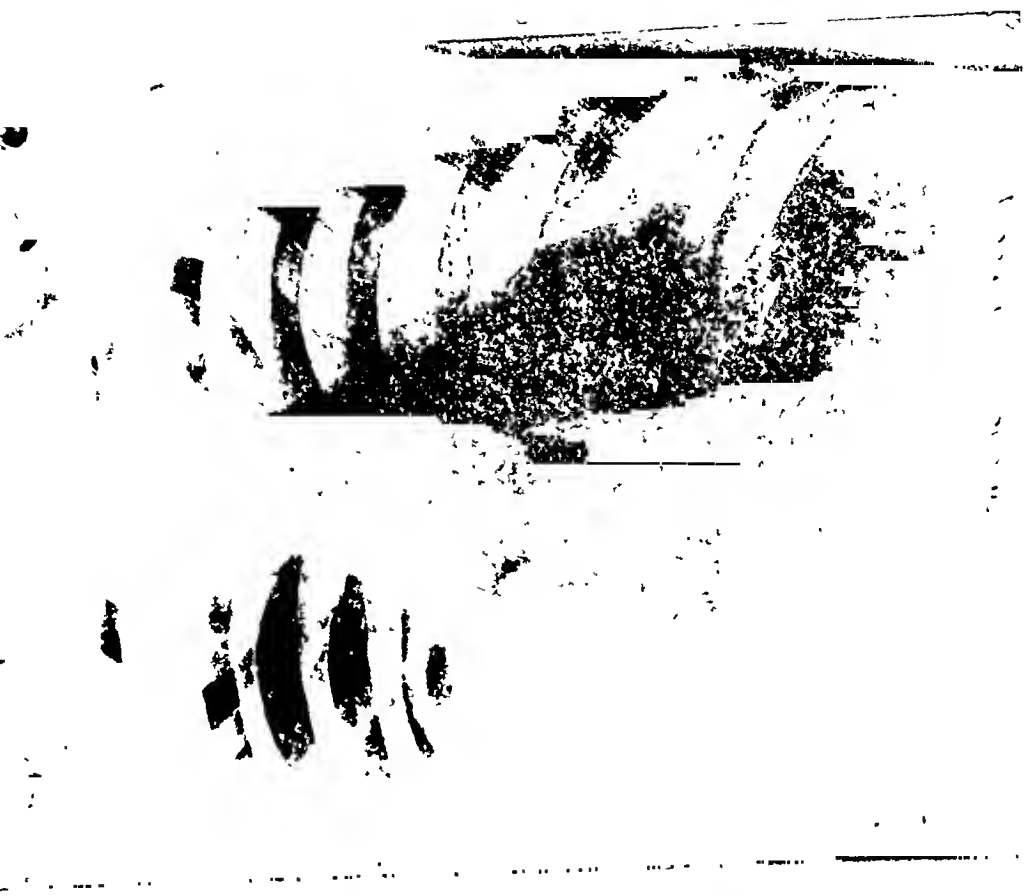


Fig. 1.—(b) A.P. view after pneumoperitoneum.

PLATE XVII

PNEUMOPERITONEUM IN THE STUDY OF HEPATIC ABSCESS : H. B. LAL. (O. A.) PAGE 90

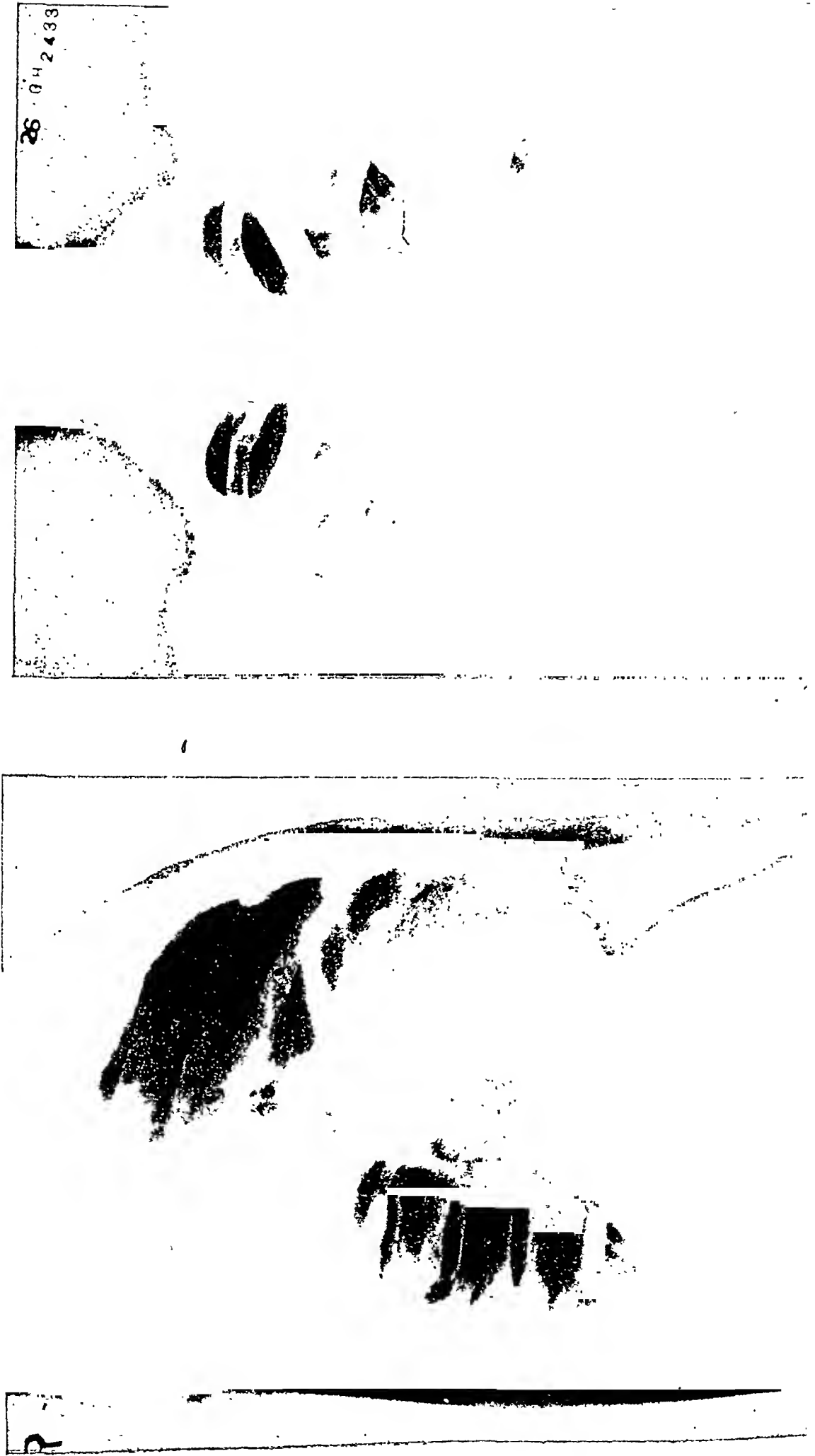




Fig. 2.—(b) A.P. view after pneumoperitoneum.

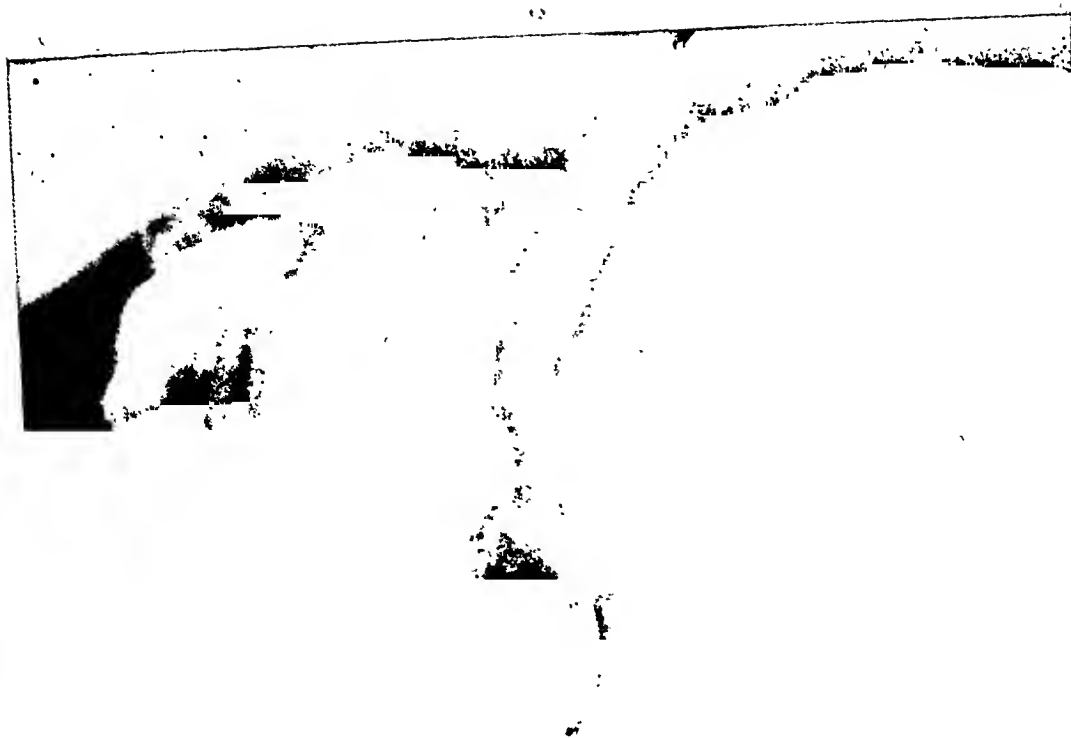


Fig. 2.—(c) Lateral view after pneumoperitoneum.

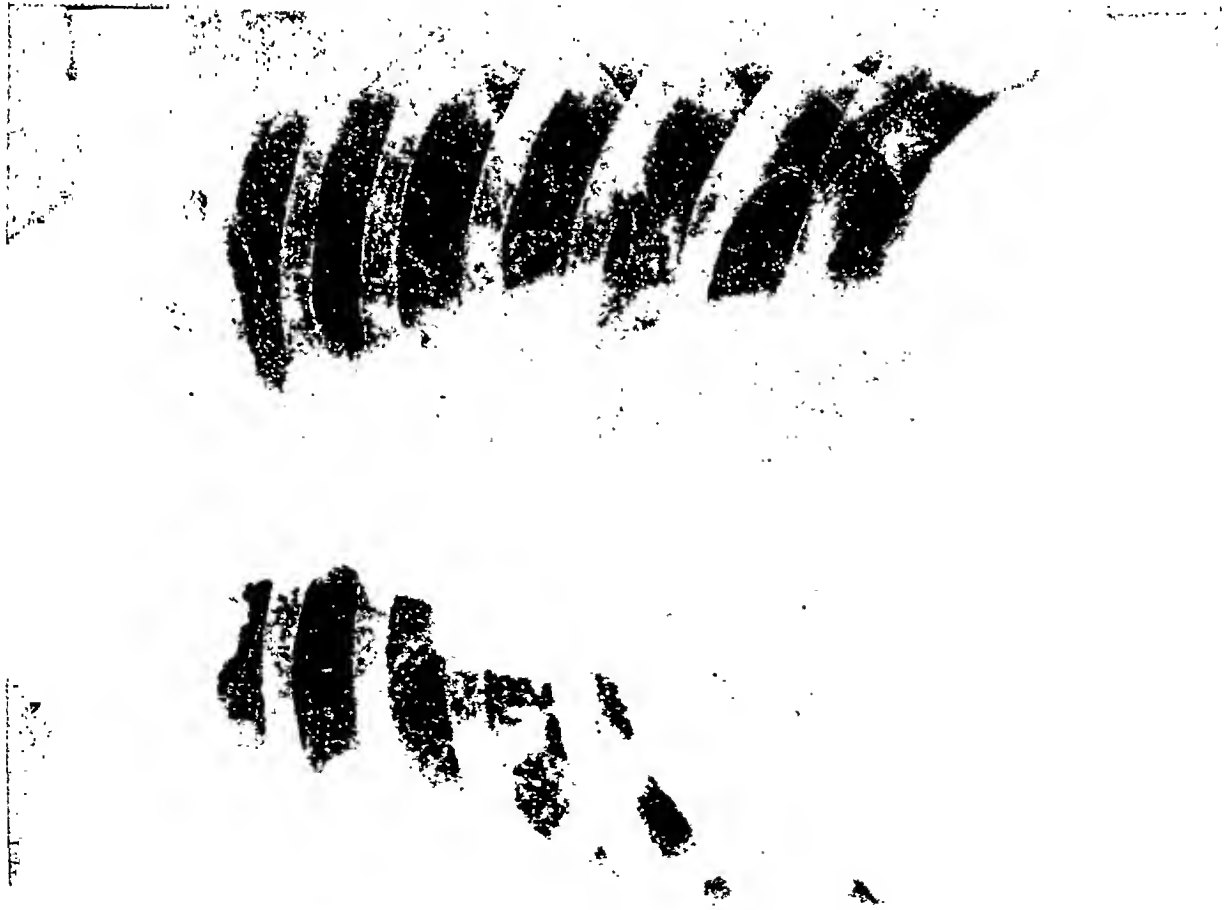


Fig. 3.—Collapse lung. (a) A.P. view.

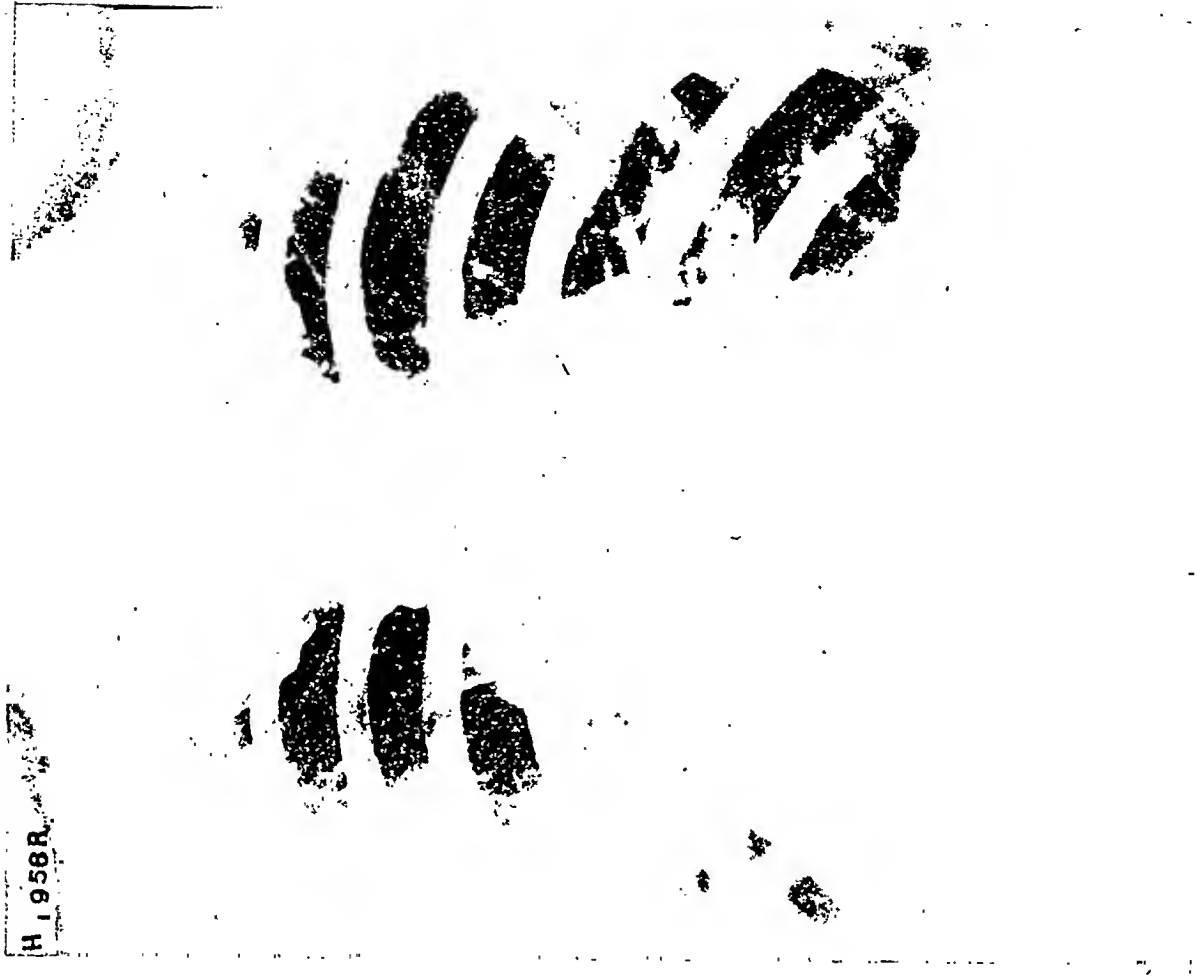


Fig. 3.—(b) After pneumoperitoneum collapse of middle and lower lobe brought out in relief.

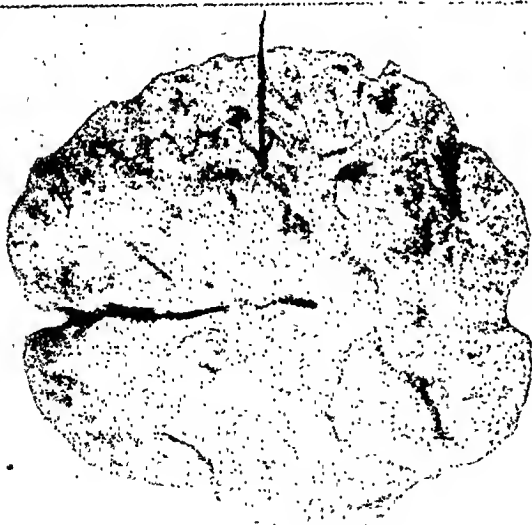
1



4



2



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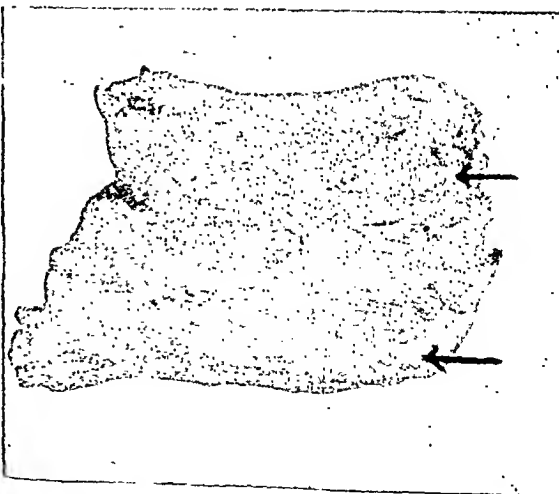
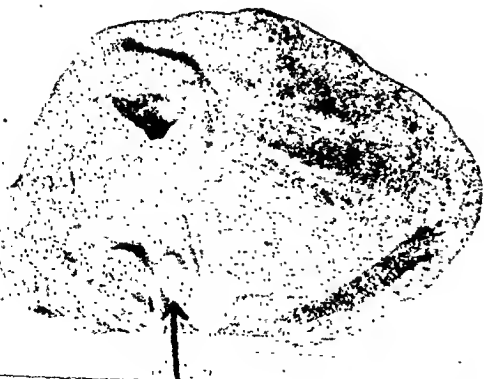




Fig. 1.



Fig. 2.



Fig. 3.

He then came under the treatment of a skin specialist who treated him for two months as a case of leprosy but the condition became more aggravated.

In the middle of July 1948, the senior writer was called in to see the case by his attending physician (P.C.T.). The patient was feeling similar pain in his right leg and ulcers were spreading. The skin adjacent to them looked black, and a little higher up it was dark red. There was foul smell. Ulcer of the great toe was very tender. A little oedema was noticed all over the part.

W.R. was negative. A diagnosis of Raynaud's disease was made. He was given nitrites, iodide, acetylcholine, Lacarnol, Depropanex, tonic and vitamins. These checked the progress, colour of the skin improved but there was no sign of healing. Pain also continued.

The case was admitted into the Campbell Hospital and was operated upon. In spite of sympathectomy, ulcers and the pain continued.

About three months after this he came to the writers again. They tried same medicines again for a month but he got no relief. Now they thought of Fibrolysin to dissolve the sclerosed tissue of blood vessels and to influence metabolism, they also gave him Antithyroidin, both the medicine prepared by E. Merek. He was given ten injections of Fibrolysin, one every other day and Antithyroidin 1 cc. daily by mouth. Ulcers healed up and pain went completely. He has been working like a normal man for the last four months.

BRIEF NOTES ON TWO CASES OF SCRUB TYPHUS FEVER WITH UNUSUAL NEUROLOGICAL SIGNS

By CAPTAIN G. S. RAO, M.B., B.S.

Salur

(Late Medical Specialist and Officer-in-charge of Scrub Typhus Research, North Burma Area, Ex-Indian Medical Service, E.C.)

Case 1

No. 160583, Sep.-Fitter Gnanamuthu, of 552 Ind. Inf. Tps. W/shop, aged 21 years, was admitted into no. 9 Ind. Fld. Ambulance on 6th July, 1945, for rigor, fever and headache of 3 days' duration. His blood slide was negative for malarial parasite but he was put on mepacrine (routine anti-malarial treatment) and alkalis. On 9th July, 1945, he complained of numbness of tongue and defective articulation from the previous night. He was then given quinine intravenously, gr. 6, with coramine and evacuated to 47 Fld. Ambulance where he was afebrile but more apathetic and aphasic

with cold extremities and dilated pupils which were reacting to light. He was conscious. On 11th July, 1945, he was given another intravenous quinine, gr. 6, and was evacuated to 58 I.G.H.(I.T.). (Prior to his present illness he was sick in hospital for a week for fever and was discharged. Since then he never felt well and reported sick once again on 6th July, 1945, at no. 9 Fld. Ambulance.)

12th July, 1945 : Condition on admission at 58 I.G.H.(I.T.)

A fairly nourished young man, not anæmic, no oedema over any part of the body, temperature 101°F., extremely apathetic, dysarthric, superficial lymph glands not enlarged, no rash, no eschar, coated and moist tongue, liver and spleen not palpable. Heart nothing abnormal detected. B.P. 100/65 mg. Hg. Lungs nothing abnormal detected. C.N.S. pupils dilated, equal and reacting to light. Urine N.A.D. W.B.C. 19,800. Blood slide for malarial parasite was repeatedly negative. Widal and Weil-Felix could not be done. Running irregular low remittent temperature ranging from 99°F. to 101°F.

Put on fluids from 16th July, 1945. He was more lively and expressed by signs that his right arm and right leg were less powerful than those on the left side.

On thorough examination of the C.N.S., the following positive signs were elicited. Speech still slurring and articulation was not clear. Paralysis of 7th cranial nerve of upper-motor neurone type. Muscular power of right arm and right leg weaker than that on left side. No loss of sensation for touch, pin-prick, sense of position or passive movement. Abdominal reflexes lost on right upper and lower quadrants. Plantar reflex flexor on both sides. 'Wartenburgh's sign' positive on the right side. All the deep reflexes (tendon reflexes) slightly brisk on the right side. Persistent ankle clonus present on the right side.

Ophthalmologist's report.—'Left fundus cedema lower and outer part'.

C.S.F.—Clear under low pressure, about 25 drops per minute. Pressure not measured by manometer. R.B.C.† 22 per c.mm. W.B.C. 9 per c.mm. Proteins 30 m.gr. per 100 cc.

W.B.C.—16,600. P. 54 L. 34. M. 11. E. 1.

Urine.—Sp. gr. 1.015. No albumin, no sugar, acid reaction.

*Dorsiflexion of the thumb occurring on flexion of the other fingers against resistance seen in pyramidal lesions. This test was done by Lieut.-Colonel Ransom, the then . . .

†The R.B.C. in the C.S.F. are not due to damage to any blood vessel during the spinal puncture. 'Reports on the spinal fluid . . . plasmocytes and erythrocytes may be found in addition (Schtefko).'

Skiagram skull.—Nil definite.

Blood culture.—Sterile.

18th July, 1945.—At this stage he was seen by the consultant physician and the neurologist and advised a course of M.&B. 760. The most probable diagnosis of cerebral abscess was made. He was put on M.&B. 760, with the usual precautions of fluid intake and output chart.

20th July, 1945.—W.B.C. 9,800. Still febrile.

23rd July, 1945.—Blood Kahn 'doubtful'.

24th July, 1945.—Afebrile. Improvement in the power of speech and power in the limbs noted.

25th July, 1945.—W.B.C. 5,800, M.&B. 760 stopped. Total dose given was 21 gm.

29th July, 1945.—General condition far better. Articulation improving.

11th August, 1945.—Fundii—no œdema. Abdominal reflexes elicited. No ankle clonus. Muscular power of right arm much improved.

20th August, 1945.—C.N.S. nil abnormal noted, except very slight slurring in the speech.

Date	WEIL-FELIX			WIDAL	
	OX2	OX19	OXK	T.O.	A.O.
1-8-45	Nil	Nil	1/250	Nil	Nil
4-8-45	Nil	Nil	1/1000	Nil	Nil
8-8-45	Nil	Nil	1/1000
12-8-45	Nil	Nil	1/1000
16-8-45	Nil	Nil	1/1000
20-8-45	Nil	Nil	1/500

Case 2

No. 18300, Sep. Zargoon Shaw of 4/15 Punjab Regiment, 35 years old, was admitted into 58 I.G.H. (I.T.) on 25th July, 1945, for a remittent fever of 7 days' duration, with generalized adenitis and tender palpable spleen with B.T. malarial infection. Had treatment with quinine before he reached 58 I.G.H. (I.T.).

Condition on admission at 58 I.G.H.—Remittent fever of 7 days' duration, apathetic, palpably enlarged post-cervical and inguinal glands which are tender, severe headache. Spleen: palpable, 1 finger breadth below the left costal margin. Heart and lungs: nothing abnormal detected. No rash, no eschar noted. Blood slide for malarial parasite repeatedly negative. Total W.B.C. = 7,800.

Urine.—Nothing abnormal detected.

Date	WEIL-FELIX			WIDAL	
	OX2	OX19	OXK	T.O.	A.O.
26-7-45	Nil	Nil	1/100	Nil	Nil
31-7-45	Nil	Nil	1/500	Nil	Nil
20-8-45	Nil	Nil	Nil	Nil	Nil
24-8-45	Nil	Nil	1/500	Nil	Nil

He was afebrile from 3rd August, 1945, and convalescing satisfactorily. From 18th August, 1945, he was more and more apathetic and showed a tendency to cry like an infant whenever a question was put to him.

20th August, 1945.—Has been afebrile. Lies listless on his back. Does not talk or even ask for food. When asked a question he would cry like an infant. Incontinent of urine and faeces. Tongue heavily coated and moist. Abdomen scaphoid and soft. Liver and spleen not palpable. C.V.S.: nothing abnormal detected. B.P. 110/70. R.S.: nothing abnormal detected. C.N.S.: pupils not dilated, equal and react to light. Fundii: normal. Moderate generalized rigidity of musculature present. Abdominal reflexes absent. Plantar reflexes markedly extensor on both sides and the deep reflexes are slightly exaggerated on both sides. Persistent ankle clonus present on both sides. No signs of paralysis. C.S.F.: clear and normal pressure, 1 cell per c.mm., protein 30 m.gr. per 100 cc., chlorides 700 m.gr. per 100 cc. Kahn: 'negative'. Blood Kahn: 'positive'. W.B.C. 7,200, P. 68, L. 26, E. 4, M. 2.

All the above signs and symptoms gradually disappeared. The earliest to do so was incontinence of urine and faeces and the last was the rigidity of the musculature. The emotional disturbance however was unsteady. It remained for a week or so continuously and disappeared only to reappear for the second time. Finally, it was not noted when the musculature got rid of its rigidity. He was convalescing satisfactorily by the time I left the case on 14th September, 1945.

Discussion

Case 1.—The hemiparesis, loss of abdominal reflexes, and paralysis of the 7th cranial nerve of the supranuclear type on the right side with dysarthria, low-grade fever, œdema of the fundus on the left side, leucocytosis and extreme apathy are the principal features. Of these, except leucocytosis and probably fever, all the other signs are highly suggestive of an intracranial mischief and a tentative diagnosis of a space-occupying lesion—a cerebral abscess—was made in the beginning. As there were numerous cases of scrub typhus fever from the same unit, his blood was also sent for Weil-Felix and the diagnosis of scrub typhus made by the regular rise and fall in the titre for OXK strain. There were none of the usually found characteristic features of scrub typhus in this case except probably extreme apathy. The irregular low remittent fever is very unlike that of scrub typhus.

Case 2.—In this case the onset of nervous signs, i.e. generalized rigidity of the musculature, incontinence of faeces and urine, loss of abdominal reflexes with bilateral Babinski's sign, persistent bilateral ankle clonus and emotional disturbance,

was during convalescence and while afebrile. That is exactly one month after the onset of fever. On 20th August, 1945, Weil-Felix OXK was nil and on 24th August, 1945, OXK titre rose up to 1/500. All these signs cleared away in the course of about 3 weeks without treatment.

Nervous signs are fairly common, rather, I should say, more common than any other, barring bronchitis. I have seen quite a few cases both in Arakan and in Burma. But the nervous signs as far as I can say from my experience (of about 100 cases in Arakan and about 250 cases in Burma, which passed through my hands and which I chanced to see from October 1944 to May 1945 and June 1945 to September 1946, respectively) comprise mostly apathy or mental dullness, headache, meningeal irritation, deafness, delirium and fine tremors of hands, lips and tongue. (As regards fundal changes I must confess I did not investigate.) But these two cases are the only ones I came across showing this type of nervous signs.

Judging from the essential pathology of the disease—that the rickettsia invade the endothelial cells of the smaller blood vessels resulting in proliferative endarteritis and perivascular infiltration with plasma cells and monocytes—any sign or symptom may be expected depending on the site of mischief, and if of nervous origin, can be distinguished as central or peripheral. 'In a Polish epidemic of 44 cases hemiplegia with or without disorder of speech characterized 22'. 'Devaux's analysis of 215 Roumanian

cases . . . shows emotional disturbance in 28 cases'.

In case 2, the blood Kahn was 'positive', but the C.S.F. Kahn was 'negative' and did not show other characteristic features of syphilis. Moreover, blood Kahn was 'positive' in scrub typhus fevers in fair per cent of cases. Though it was observed that previously existing organic affection was aggravated by typhus (Devaux's analysis of 215 Roumanian cases shows 2 existing organic affections aggravated by typhus). In this particular case syphilis can easily be ruled out. In a proved case of typhus the above-mentioned nervous signs and symptoms had their onset during convalescence and disappeared well within a month without treatment. 'Psychotic syndromes may develop during convalescence' (Skliar). But the sort of emotional instability observed in case 2 during the convalescence, though evanescent, I think, could be compared to the emotional instability which is seen as one of the after-effects of 'epidemic encephalitis'. Is it possible that in this particular case it is a manifestation of post-typhus encephalitis?

I wish to thank the DG, AFMS, for permitting me to report this note and also Lieut.-Colonel S. M. Basu for encouragement.

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Therapeutic Notes

NOTES ON SOME REMEDIES

XXXIII.—DEHYDRATION AND ITS TREATMENT

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Part IV. Dehydration in Infants—contd.

Treatment of infantile diarrhoea and vomiting

THE following details of treatment are meant to serve as a guide and should be varied to suit the special needs of infants, as each case requires separate consideration. The child should be under frequent observation as its condition may undergo rapid alteration in a short time. Skilled nursing is an important part of treatment.

General.—No purgative is usually required as the diarrhoea has been sufficiently severe to empty the intestinal tract. Gastric lavage and colonic irrigation may be of great benefit by washing out the mucus. No milk feeds should

be given for a period varying from 18 to 24 hours, or longer, during which it is of course essential that fluid (saline and glucose) should be administered by mouth or infusion. The food chosen should be low in fat and gradually introduced. Fat predisposes to vomiting by delaying gastric evacuation, and the unabsorbed fatty acids in the intestine cause further irritation. Fresh milk even, when well diluted, is usually not well borne during the acute stage. One may start with whey, skimmed dried milk or lactic acid milk and then give half cream and later full cream milk as the condition improves. Preparations like Benger's or Savoy and Moore's Food or Horlick's milk, suitably diluted, may be helpful when other foods are found unsuitable. As sugar is likely to cause flatulence from intestinal fermentation and thus aggravate the condition a little saccharin may be added to sweeten the fluid during the early period of the treatment.

Diarrhoea is not common in breast-fed infants, and when it occurs, all that is required is the partial or complete discontinuation of breast feeding for 12 to 24 hours, during which glucose in saline is given and the mother's breasts are emptied at regular intervals by artificial means. When nursing is resumed, it should be limited to 4 or 5 minutes, and the intervals to 4 hours, water or glucose being given between each nursing. If diarrhoea or vomiting is severe, the management is identical with that for artificially fed infants.

Management.—The following directions apply to an infant one year old or under :

1. *When the infant is not dehydrated.*

(i) No milk feeds for 18 to 24 hours, during which half-normal saline is given by mouth every two hours at the rate of $2\frac{1}{2}$ oz. per lb. per day.

(ii) After this period give dilute milk feeds, e.g. half cream dried milk $2\frac{1}{2}$ oz. per lb. per day. Extra fluid in the form of water should also be given.

(iii) If this is well tolerated, gradually increase the strength and size of the feeds.

(iv) As the stools become normal, gradually change to full cream dried milk, e.g. by replacing part of the half cream by full cream milk every other day.

(v) If diarrhoea recurs repeat the same treatment.

2. *When dehydration is present.*

(a) *Mild or moderate cases.*—Same treatment as given above if the child's general condition is good. In addition to the usual allowance of fluid, give 5 to 10 oz. per day for correcting the fluid deficit.

(b) *Severe cases.*—(i) Give intravenous half strength Hartmann's solution containing 5 per cent glucose by continuous drip during the first two hours at the rate of 20 drops per minute (about 70 to 80 cc. per hour) and later at 10 drops per minute; the rate of flow should be judged in each case individually.

(ii) When there has been much loss of salt from vomiting or diarrhoea, give normal saline or full strength Hartmann's solution with glucose at first, and after about one-fifth of the total fluid requirement for the day has been administered, continue as in (i).

(iii) When the immediate danger of dehydration is over (about 12 to 24 hours), give plasma (10 cc. per lb. of body weight) with equal part of half strength Hartmann's solution and glucose.

(iv) Continue the drip, repeating the plasma at least once in 24 hours, until diarrhoea has ceased or greatly decreased, dehydration is corrected and the infant is able to take fluid by mouth.

(v) Do not give more than 20 oz. (600 cc.) of fluid in 24 hours intravenously to an infant

under 6 months. Also be careful of giving it in excess when bronchitis or other respiratory disease is present. The appearance of œdema of the scrotum, vulva, feet, hands and eyes or over the tibia is a sign of excess of fluid being given.

(vi) If continuous intravenous injection cannot be arranged, give it at suitable intervals.

(vii) If subcutaneous or intramuscular injections are required, normal saline or Hartmann's solution is used either as a single injection of 50 to 100 cc. 6-hourly or by drip at the rate of 3 to 10 drops per minute (12 to 40 cc. per hour).

(viii) If signs of anoxæmia are present, e.g. cyanosis or pallor, administer oxygen.

(ix) If under conditions known to cause hæmoconcentration the red blood cells are below $2\frac{1}{2}$ million or hæmoglobin below 50 per cent, whole blood transfusion is indicated, but only after hæmoconcentration has been corrected.

(x) If parenteral infection is present, e.g. broncho-pneumonia, otitis media and pyelitis, give sulphadiazine 0.5 gm. 4-hourly for 5 days. It may be combined with penicillin (20,000 to 40,000 units 4-hourly). The latter is preferable if urine is scanty.

(xi) Streptomycin has been very effective in some cases. James and Kramer (1948) gave the drug by mouth to a number of children with gastroenteritis in whose stool *Proteus vulgaris* was present. The total dose of streptomycin was usually 2 gm. administered over a period of 7 days, 0.5 gm. being given in the first 24 hours and 0.25 gm. on each of the 6 subsequent days. It was given before each feed with 1 cc. of sterile water. They also found it effective where no pathogenic organisms are found. There is, however, the danger that the small amount of streptomycin that is absorbed from the gut may render pathogens elsewhere (e.g. in urinary infection, mastoiditis) streptomycin resistant, though these may respond to penicillin or sulphonamides.

(xii) *Feeds.* For the first 18 to 24 hours the infant is allowed $\frac{1}{2}$ oz. of half strength Hartmann's solution sweetened with saccharin two-hourly to keep the mouth moist. Thereafter small feeds of 1 oz. of half strength Hartmann's solution are given, followed by gradual building up of milk feeds as already indicated. Full cream milk should not be given too soon. Over-feeding should be avoided during convalescence since it may cause a relapse which often is harder to treat than was the original attack. Lactic acid milk is valuable at such times.

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Indian Medical Gazette

MARCH

PARA-AMINOSALICYLIC ACID : PAS

THIS important advance in chemotherapy of tuberculosis has remained unsung in our pages so far and yet it is superior to the preparations of gold which gripped the imagination of the medical and non-medical world alike some 25 years ago. The songs sung in its praises elsewhere have not been very loud either. Probably the failure of the gold preparations has contributed to the lack of fervour shown to this drug.

Acceleration of respiration in the bacillus of tuberculosis.—It was observed ten years ago that sodium salicylate increases the oxygen consumption and carbon dioxide production of the tubercle bacillus (Bernheim, 1940). Sodium benzoate produced a similar, though less effect. These chemicals were evidently concerned in the metabolism of the bacillus: both of them weakened the bacillus by increasing its katabolism. The benzoate, however, was found to inhibit the action of the salicylate.

Bacteriostatic effect.—Later, a systematic search was commenced for a substance derived from the series which would have a definite bacteriostatic action on the bacillus. Some 50 substances were tried (Heaf and Rusby, 1948). The most active substance found was 4-aminosalicylic or para-aminosalicylic acid. In a concentration of 0.15 mg. per 100 cc. it inhibited the BCG strain *in vitro*.

Early animal experiments with PAS.—*In vivo* experiments on mice and guinea-pigs confirmed the hopes raised by the *in vitro* experiments. The drug retarded the development of experimental tuberculosis (Editorial, 1949).

PAS and streptomycin.—The combined effect of the chemical and streptomycin was studied, in animals, next. Both acting together produced a 'much more favourable effect' than either drug acting singly (Lehman, 1946).

The possibility of reducing the dose of streptomycin and thus reducing or eliminating the toxic effect was also suggested. Further, a check on the production of the streptomycin-resistant strain became possible and was demonstrated.

Treatment of human cases.—Actual cases of pulmonary tuberculosis were treated first in Stockholm with doses of 14 gm. daily for 1 to 6 months, alongside an equal number of controls. The toxic reaction, no more than diminution in appetite, nausea and vomiting, was negligible.

Improvement in the general condition of the patient was noticeable. None, however, became free from tuberculosis.

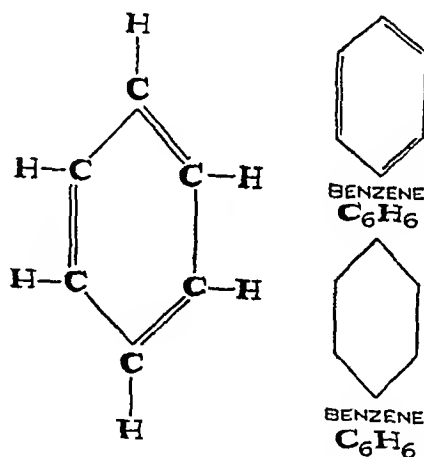
Further trials elsewhere with 10 to 11 Gm. of the chemical daily, in 3 to 5 doses, by mouth for 3 consecutive weeks with an interval of one week also showed improvement. Fever, cough and expectoration improved within a week. Radiological improvements have been recorded. Hardening and retraction of apical lesions, diminution in the size of the cavities and clearing of areas of soft mottling have occurred (Erdie, 1948).

Bacilli have disappeared from sputum (Tidy and Short, 1949).

Preparations for subcutaneous, intramuscular and intravenous administration are available (Heaf and Rusby, *loc. cit.*; Tidy and Short, *loc. cit.*). It has been suggested that a daily dose of not less than '20 to 25 Gm' should be continued for at least 3 months (Erdie, *loc. cit.*). A 'course' in Calcutta costs to-day about Rs. 100. The cost is bound to come down like that of streptomycin which to-day can be had at one-fifth of the price charged 2 years ago.

Intrapleural use.—10 cc. of a 20 per cent solution weekly has not proved a success (Tidy and Short, *loc. cit.*).

Chemical considerations.—To go back to the earlier years in medical studies, both salicylic acid and benzoic acid are benzenic derivatives. Benzene is a carbocyclic hydrocarbon. In it 6 carbon atoms combine in the form of a hexagon with alternate single and double bonds, and to each carbon atom is also attached a hydrogen



Three ways of representing the benzene ring.

atom. Replacement of the hydrogen atoms by other atoms results in many well-known compounds, thus :

Benzene minus H plus OH = Phenol

Benzene minus 2H plus 2OH = Resorcinol

Benzene minus 2H plus OH plus CH₃ = Cresol, ortho, meta and para depending on the nearness of the CH₃ to the OH.

Benzene minus H plus COOH = Benzoic acid
 Benzene minus 2H plus OH plus COOH = Salicylic acid
 Benzene minus 2H plus O-OCCH₃ plus COOH = Acetyl salicylic acid

The first is the standard antiseptic and the last a common drug used by millions of people all over the world as aspirin. Over 5,000 tons of it are produced annually in the United States of America alone (Routh, 1949).

The PAS is benzene minus 3H plus NH₂ plus OH plus CO₂H. It may be looked upon as a special aspirin which is not quite so easy to prepare as the ordinary aspirin but does not involve the expense and secrecy of folic acid or vitamin B₁₂.

It is made commercially from meta aminophenol (which is readily prepared from benzene) by the action of CO₂ under pressure.

Incidentally, work on the tuberculostatic substances which are derivatives of *p*-aminobenzoic acid is in progress (Jensen and Ploug, 1949). Better and cheaper substances may be available soon.

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POLIO YET AGAIN

THE U.S.A. death rate for 1948, published under 'Medical News' in this issue on page 109, shows that the death rate for poliomyelitis and acute polioencephalitis increased from 580 in 1947 to 1,895, over three times, in 1948. To us it appears that the disease is assuming a pandemic form and has caused deaths even in India where ordinarily, in common with other organic diseases of the nervous system, it is rather a tame affection on the whole. The deaths believed to be caused by encephalitis lethargica and cryptogenic rabies, commented upon in these pages, might easily have been caused and were probably caused by poliomyelitis (polioencephalitis).

Incidentally, polio, as we have stated already, has nothing whatsoever to do with insanitation. At least its incidence is not favoured by insanitation. It has even been thought that the incidence might be favoured by sanitation. We repeat these observations in view of recent communications from responsible quarters to the contrary. Those interested in the disease will recollect the communications. Any funds spent under this excuse will be wasted or may even favour the incidence of the disease.

Medical News

ANTITETANUS INOCULATION

(Abstracted from *British Medical Journal*, Saturday, 3rd December, 1949, p. 1305)

UNDER 'Any Questions?' the following note appears:—

Two injections, each of 1 ml. of tetanus toxoid, with a six-week or longer interval, give a good immunity to tetanus in most individuals, but the level of measurable antibody drops fairly quickly during the next year, and for those exposed to the risk of tetanus, a boosting dose should be given six to twelve months after the primary course. The response to the boosting dose is most striking. The antitoxin titre shoots up to 10 antitoxin units or more (100 times as high as that following the primary course) and is usually maintained at a high level for many months. In the services this stimulating dose should be given to personnel before they are engaged in active operations. If an actively immunized person suffers a wound or injury, there is the choice of giving a dose of tetanus antitoxin which provides immediate protection, or of tetanus toxoid which stimulates the production of fresh antibody within three to five days, or of both antitoxin and toxoid.

INDIA SETS UP POPULATION INSTITUTE

(Reproduced from UNESCO Features, No. 16. 1st March, 1950, p. 4)

INDIA, homeland of one-sixth of the world's inhabitants, is establishing an institute for the study of population statistics. Dr. S. P. Chandrasekhar, until recently in charge of population research at UNESCO, is the founder and will be the director of the institute, the first of its kind in India.

It will function under the auspices of the Annamalai University where Dr. Chandrasekhar is head of the economics department. In addition to studying all aspects of Indian and Asiatic demographic problems, it will act as a co-ordinating centre for the researches of social scientists.

WORLD HEALTH ORGANIZATION FELLOWSHIPS

(Reproduced from *British Medical Journal*, Saturday, 10th December, 1949, p. 1363)

THE World Health Organization, in order to strengthen health services throughout the world, provides fellowships to medical practitioners who are engaged,

or will be engaged, in public health services, medical education, or medical research. The amount of the fellowships varies from 200 to 300 dollars a month, plus cost of travel, tuition fees, books and literature. The fellowships are open to members of the medical profession who have gained at least two years' experience in the field in which they will study under the fellowships scheme. In special circumstances consideration will be given to undergraduates and to non-national graduates employed by the governments of countries not possessing their own graduates suitable for fellowships, provided that such fellows agree to return at the end of their period of study in order to serve the country whose government sponsored their fellowship. Full details of the fellowships can be obtained from the General Secretary, United Nations Organization, Palais des Nations, Geneva.

HOW THE DEAF MAY 'HEAR THROUGH THEIR FINGERS'

(Reproduced from *Science and You*, by MAURICE GOLDSMITH, UNESCO Science Editor, UNFSCO Features, No 16, 1st March, 1950, p 12)

A GLOVE worn on the left hand may break the black curtain of silence that cuts off the deaf person from his more fortunate neighbours. Though the fingers will come sound and the possibility of developing normal social intercourse.

That is the high hope raised by experiments now being carried out by an American mathematician. He is Dr Norbert Wiener, Professor of Mathematics at the Massachusetts Institute of Technology. In 1948, he startled the world with a revolutionary mathematical concept of the brain and machines termed *Cybernetics**—'the science of control and communication in the brain and in the machine'. The prospect of rescuing many deaf persons from their prison of silence is only one of the likely consequences of this new scientific outlook.

Dr Wiener believes that the way in which a machine functions has certain elements in common with the way in which the human nervous system works. He is seeking a theory which will explain control and communications not only in machines, but also in living organisms. An eye has often been compared with a camera, and an ear with a telephone receiver. Knowledge of the eye and ear, in fact, have helped the development of the camera and the telephone. Now, however, the possibility of a two-way flow between the mechanical and biological sciences is being more fully explored than before.

An example of the way in which Dr Wiener is developing this new field of science is in his examination of deafness and blindness. These are defects of the senses, that is, defects which hinder and interrupt the reception and communication of impressions from the world around. 'In order to make any effort to replace the lost senses', argues Dr Wiener, 'it is necessary for us to make a rather accurate measure of what they have lost. It is then necessary for us to see if there are any relatively unused channels into the human nervous system which are capable of supplying the whole or any considerable part of what is lost. These are problems of physiology and communication engineering, and have a most important mathematical side.'

Research by technicians at the Bell Telephone Laboratories, and other, suggested that there might be such 'unused roads' to the nervous system of the deaf. They revealed that there is a great loss of information in the process of transmitting a message to the ear; that a crude imitation of speech involving

less than one-tenth, and perhaps even one-hundredth of the information carried over a telephone line is enough for adequate conversation.

This led Dr Wiener to the view that 'the recognizable part of speech was so scanty, that it was not beyond our hope to replace it by the sense of touch, backed up with adequate equipment. In other words, it appeared to us that it is perfectly possible to make the transition between sound in the outside air, and the semantic* recognition of speech, by an artificial phonetic stage, making use of touch, and supplemented by adequate electrical tools'.

A machine was constructed, and some experiments made with a blind deaf mute and his brother. Normally, when they wished to speak to each other, the deaf mute placed his hands on his brother's larynx. He could then 'feel' what was being said. The deaf mute could pronounce a few words, but they were 'very breathy and bad'.

He was put in the apparatus, and for the first time in his life he was able to compare his brother's speech with his own. 'Within a matter of minutes, and certainly of hours, the improvement in his enunciation was not merely noticeable, but overwhelming. It was perfectly clear to us that our apparatus is an adequate way for a deaf mute, even for a blind deaf mute, to monitor his own speech', says Dr Wiener modestly.

This apparatus translates sound waves into electric vibrations which can be felt by the deaf through the fingertips and interpreted into meaningful words. It is at the moment a large and crude machine: the aim is to re-design it in the form of a glove.

The device receives sound waves between 100 and 3000 cycles through a microphone. Wave filters break the cycles into five frequency channels each comprising one octave. Five separate vibrators receive the frequency bands and oscillate accordingly. With each finger inserted into a vibrator, the deaf subject can be taught to recognize the individual patterns produced by different words and thus build up a competent vocabulary.

Teaching the deaf, a new vocabulary should be no more difficult than teaching a normal child to speak. The deaf would be taught by pointing to a written word or object, speaking the words and then having him feel the pulse across his fingertips that the word produces.

There is hope also for the blind in these researches into methods of communication (although not immediately), and for the crippled.

For the blind, for example, the possibility is envisaged of a reading machine which will translate the pages of an ordinary book into a sound or touch pattern which can be recognized by them.

For the crippled the aim is to devise a 'support' for the limb which will enable impressions to be received from the outside world and thus improve the functioning of the crippled person. For, the cripple has lost not only movement through the limb, but also sensation.

Thus, from this theory of the mathematician, there is the prospect of returning to useful life those who, up to the present, have been regarded as useless to—and a burden on—society.

DEATH RATE IN THE UNITED STATES

(Reproduced from Release No. FSA716, issued by Federal Security Agency, Public Health Service, Washington 25, D.C., dated 24th December, 1949)

THE death rate for the United States in 1948 was the lowest in the history of the country, John L. Thurston,

*Cybernetics—a word derived from the Greek *kubernetes*, meaning steersman

*Semantics—the interpretation of the meaning of words

Acting Federal Security Administrator announced to-day. The announcement was based on a compilation just completed by the Public Health Service's National Office of Vital Statistics.

The crude death rate for 1948 was 9.9 per 1,000 population—2 per cent below the rate of 10.1 for 1947 and 1 per cent lower than the 1946 rate, the previous record low, the report showed.

The leading causes of death remained the same as in 1947. The major chronic diseases associated with advanced age accounted for 63 of every 100 deaths. Death rates in this group showed only slight changes from the 1947 record. The death rate for diseases of the heart was 322.7 per 100,000 population, while the 1947 rate was 321.2. The death rate for cancer and other malignant tumours increased from 132.4 in 1947 to 134.9 in 1948. The death rate for diabetes remained about the same for the two years; the 1947 rate was 26.2 and the 1948 rate 26.4. Deaths from nephritis, and from intracranial lesions of vascular origin, each showed small declines. The 1948 death rate for intracranial lesions was 89.7, while the 1947 rate was 91.4. The nephritis death rate dropped from 56.0 in 1947 to 53.0 in 1948.

Mortality from the major infectious diseases continued their long-term declines. The death rate for pneumonia and influenza combined, and the rate for tuberculosis both reached new lows. A 10 per cent decline from the 1947 rate brought the death rate for

tuberculosis (all forms) for 1948 down to 30.0 per 100,000 population and the rate for pneumonia and influenza down to 38.7.

Motor-vehicle accident deaths decreased for the second successive year. The rate for 1948 for this cause was 22.1 per 100,000 population, while the 1947 rate was 22.8. The death rate for accidents other than motor-vehicle accidents also decreased from the 1947 rate of 46.6 to 45.0 in 1948.

Mortality from two of the communicable diseases of childhood increased sharply from 1947, a low year. The number of deaths from poliomyelitis and acute poliomyelitis increased from 580 deaths in 1947 to 1,895 deaths in 1948, bringing the death rate back up to the 1946 level of 1.3 deaths per 100,000 population. Deaths from measles rose from 472 in 1947 to 888 in 1948, which was still well under the figure of 1,310 recorded for 1946. Deaths from whooping cough fell from 1,954 in 1947 to 1,146 deaths in 1948, continuing a long-term decline. Diphtheria deaths, also continued their decline, reversed temporarily in 1945; 634 deaths were reported from this cause in 1948.

The number of deaths and the death rates for selected causes in the United States in 1948 and 1947 are shown in the table. The numbers of deaths are exclusive of deaths among the armed forces overseas; the rates are computed per 100,000 estimated population excluding armed forces overseas.

TABLE

FEDERAL SECURITY AGENCY, PUBLIC HEALTH SERVICE, WASHINGTON 25, D.C.

Number of deaths and death rates for selected causes: United States, 1947 and 1948

(Exclusive of stillbirths and of deaths among armed forces overseas. Rates per 100,000 estimated mid-year population excluding armed forces overseas)

Cause of death	Number		Rate	
	1948	1947	1948	1947
All causes	1,444,337	1,445,370	988.5	1,007.9
Typhoid and paratyphoid fever	233	325	0.2	0.2
Cerebrospinal (meningococcus) meningitis	873	917	0.6	0.6
Scarlet fever	68	107	0.0	0.1
Whooping cough	1,146	1,954	0.8	1.4
Diphtheria	634	799	0.4	0.6
Tuberculosis (all forms)	43,833	48,064	30.0	33.5
Dysentery	1,078	869	0.7	0.6
Malaria	170	214	0.1	0.1
Syphilis	11,616	12,671	8.0	8.8
Measles	888	472	0.6	0.3
Poliomyelitis, poliomyelitis (acute)	1,895	580	1.3	0.4
Cancer and other malignant tumours	197,042	189,811	134.9	132.4
Acute rheumatic fever	927	1,024	0.6	0.7
Diabetes mellitus	38,638	37,515	26.4	26.2
Pellagra (except alcoholic)	606	728	0.4	0.5
Intracranial lesions of vascular origin	131,036	131,039	89.7	91.4
Diseases of the heart	471,469	460,580	322.7	321.2
Pneumonia (all forms) and influenza	56,493	61,836	38.7	43.1
Diarrhoea, enteritis, and ulceration of the intestines	8,831	8,069	6.0	5.6
Nephritis	77,377	80,288	53.0	56.0
Diseases of pregnancy, childbirth, and the puerperium	4,122	4,978	2.8	3.5
Congenital malformations and diseases peculiar to first year (except premature birth)	41,704	44,570	28.5	31.1
Premature birth	39,085	41,053	26.7	28.6
Suicide	16,354	16,538	11.2	11.5
Homicide	8,536	8,555	5.8	6.0
Motor-vehicle accidents	32,259	32,697	22.1	22.8
Other accidents	65,742	66,882	45.0	46.6
Senility, ill-defined and unknown causes	27,291	27,556	18.7	19.2
All other causes	164,391	164,679	112.5	114.8

[The following 6 items are reproduced from Press Releases issued by World Health Organization, Regional Office for S.-E. Asia.]

SIGNING OF AN AGREEMENT BETWEEN W.H.O. AND THE GOVERNMENT OF CEYLON

(SEA/PR/50-S, dated New Delhi, 17th February, 1950)

An official agreement between the Government of Ceylon and the World Health Organization was signed this morning in New Delhi by Mr. C. Coomaraswamy, Ceylon High Commissioner and Dr. C. Muni, W.H.O. Regional Director for South-East Asia.

The Agreement lays down the conditions under which W.H.O. will provide technical and advisory assistance or other services to strengthen and still further improve the national medical and sanitary services of Ceylon.

According to the general terms of the Agreement, W.H.O. will be responsible for the international staff and, if necessary, the whole or a part of the supplies and equipment needed for performing the W.H.O. services requested by the Ceylon Government.

The Ceylon Government will in general be responsible for expenditure in national currency incurred in connection with W.H.O. projects. This includes accommodation, subsistence costs of international staff, transport within the country and, in certain cases, part of the necessary supplies and equipment. In addition, Ceylon will provide the requisite local auxiliary staff.

The Ceylon Government also undertakes to grant certain privileges and immunities to W.H.O. and its employees engaged on projects in Ceylon, including immunity from taxation.

Under the terms of the Agreement, the nature and period of operations of each W.H.O. project shall be determined by special arrangements between the parties.

The Agreement may be terminated on either side at the end of any calendar year subject to three months' notice.

The assistance Ceylon has requested from W.H.O. in 1950 includes the provision of international teams to demonstrate modern methods for the control of malaria and venereal disease, technical aid in perfecting tuberculosis control measures, and a number of W.H.O. Fellowships.

At present a W.H.O. Filariasis Consultant is advising the Ceylon Government on the implementation of recommendations made following a filariasis survey of the island made by W.H.O. in 1949.

The necessity or advisability of undertaking a campaign for the eradication of malaria in the island is at present being explored by a W.H.O. malaria expert. If his report is favourable, the eradication project will probably be directed by a W.H.O. international team.

A goitre survey of certain areas in Ceylon is at present being undertaken by another W.H.O. expert.

EXPERTS ADVISE ON TRAINING MEDICAL AND HEALTH PERSONNEL. GREATER EMPHASIS ON SOCIAL AND PREVENTIVE MEDICINE NEEDED

(SEA/PR/50-9, dated New Delhi, 20th February, 1950)

A drastic revision of medical school programmes in order to train students in the social and preventive as well as the curative aspects of modern medicine was recommended by an Expert Committee called together by the World Health Organization in Geneva last week. Attended by experts from Chile, Belgium, Brazil, India, England, Turkey, Yugoslavia, France, Sweden

and the U.S.A., the Committee met for six days to suggest measures for improving the professional and technical education of medical and auxiliary personnel, both in advanced and under-developed countries.

The shortage of doctors and other health workers is a grave problem throughout the world, especially in Africa and Asia, and in the rural areas of Europe and America.

The Indian member of the Expert Committee was Dr. C. K. Lakshmanan, Director, All-India Institute of Hygiene and Public Health, Calcutta.

The rôle of the physician in modern society and his responsibility from the sociological as well as from the medical point of view has changed considerably in the past few decades, the Committee found. It is now generally agreed that the factors necessary for building up a healthy society include economic and social security, nutrition, housing and general health education for the public.

In most countries, medical training is apt to neglect these factors, and, according to the Committee 'by the end of their medical education, students have learnt at once too much and too little'. The report adds: 'In most areas, the undergraduate medical curriculum is inadequate and ill-balanced'.

One of the essential tasks of the World Health Organization is to establish basic standards of training for the practice of public health, the experts decided. The main emphasis in undergraduate teaching should be 'to produce medical men who can practise diagnosis and prevention, social as well as clinical pathology, and psychosomatic medicine' the Committee stated, pointing out that at present, disproportionate emphasis is given to curative medicine in the curriculum, to the neglect of social medicine.

The Committee noted a report stating that in an average urban or semi-rural area, health needs should be met by at least one general practitioner to 1,500 population, one surgeon to 10,000, one psychiatrist to 100,000 and at least 45 other public health officials, excluding auxiliary workers. In many countries the ratio is estimated to be one physician to, at best, 12,000 people or more. The areas where this figure applies are inhabited by about half the world's population.

The Committee recommended various measures to increase the availability and improve the training of various categories of medical and auxiliary personnel (doctors, nurses, industrial and medical social workers, sanitary engineers, public health dentists, statisticians, hospital administrators, laboratory workers, health educators, nutritionists, etc.).

W.H.O.'s programme in this field will include assisting countries to develop their medical schools and other teaching institutions, organizing group training for health workers in various regions, awarding fellowships to senior teaching staff, training local health personnel with W.H.O. demonstration teams and providing experts and lecturers to develop teaching methods and technical training in public health, tuberculosis and VD control, and mother and child health, etc.

AFGHANISTAN MONARCH VISITS W.H.O. GENEVA HEADQUARTERS

(SEA/PR/50-10, dated New Delhi, 24th February, 1950)

KING MOHAMMED ZAHIR of Afghanistan on Wednesday evening visited W.H.O. Headquarters in the Palais des Nations, Geneva, where he conferred with Dr. Brock Chisholm, W.H.O. Director-General. The monarch was accompanied by high officials including the Afghan Ambassador in Paris and Professor Pierre Boulenger, Dean of the Kabul Medical School.

King Mohammed Zahir expressed his gratitude for the assistance W.H.O. has rendered to his country during the past year and explored with Dr. Chisholm the possibility of initiating new programmes in Afghanistan under W.H.O. auspices.

The King explained that he and his advisers believed that malaria control was the most important of the country's health needs.

W.H.O. programmes in Afghanistan are administered by the S.-E. Asia Regional Office of W.H.O. Last year they included a malaria survey and malaria control team in the Laghman district, a venereal disease survey, expert advice and assistance in fighting the ever-present typhus menace. At the beginning of February, Dr. K. L. Malhaustra of the New Delhi Municipal Health Services, went to Afghanistan for W.H.O. on a three months' assignment to supervise typhus-control measures. Supplies of DDT insecticide powder and dust guns were procured by W.H.O. during 1949 for the Afghan Government's anti-typhus campaign.

Besides the assistance requested in continuing and enlarging malaria control operations, Afghanistan has asked W.H.O. for expert advice concerning the development of its medical education facilities. In addition the United Nations International Children's Emergency Fund (UNICEF) has also allocated \$100,000 for Afghanistan. This will probably be used in promoting venereal-disease control and maternal and child health services in Afghanistan with technical advice from W.H.O.

King Mohammed Zahir, who is on a incognito visit to Switzerland, left Geneva immediately after his visit to W.H.O. Headquarters.

INDIA AIDS BURMA TO FIGHT SMALLPOX

(SEA/PR/50-11, dated New Delhi, 28th February, 1950)

A REGULAR weekly supply of 70,000 doses of smallpox vaccine to help in stemming smallpox outbreaks in Burma has been promised by the Indian Health Services, it was learnt this morning at the South-East Asia Regional Office of W.H.O. in New Delhi. It is understood that the vaccine will be sent each week from the Belgaum Vaccine Institute, Bombay, to the West Bengal Vaccine Institute, whence it will be collected by the Burmese Consul in Calcutta for air-shipment to Rangoon.

W.H.O. has also ascertained that additional supplies of vaccine, if needed by Burma, can be provided by the Government of Ceylon.

In the first seven weeks of 1950, a total of 2,720 cases of smallpox and 939 deaths were reported from Burma. This is more than five times the figures for the corresponding period last year. Present smallpox outbreaks appear to be most severe in Bassein where in one week during February 147 cases and 68 deaths are said to have occurred. In Rangoon during the same week, there were 105 cases and 37 deaths. Other localities affected are Danubyu, Henzada, Myaungmya and Monywa.

The Burmese Health Services are undertaking an intensive vaccination campaign in the affected areas. The gravity of the outbreak is attributed in part to a heavy influx of refugees from insurgent areas.

A first emergency air-shipment of 70,000 doses of vaccine was made last week from India, following an urgent request for assistance received through W.H.O. from the Burmese Embassy in New Delhi.

TURKEY TO INTENSIFY FIGHT AGAINST TUBERCULOSIS

(SEA/PR/50-13, dated New Delhi, 7th March, 1950)

THE Turkish Health Ministry has allocated 200,000 Turkish pounds towards the establishment of an Anti-tuberculosis Demonstration and Training Centre to be constructed in Istanbul, according to a cable from Turkey received at the W.H.O. Regional Office for the Eastern Mediterranean, Alexandria (Egypt). The Ministry's allocation will be matched by the donation

of a similar sum by the Anti-tuberculosis League of Istanbul to provide the 400,000 Turkish pounds necessary for the project.

Preliminary discussions on the setting up of this anti-tuberculosis centre in Istanbul took place when a W.H.O. Tuberculosis Consultant visited Turkey for two weeks during February. It was then decided that W.H.O. should provide technical guidance and a team of tuberculosis experts to supervise the proposed centre. The principal aim is to enable doctors, nurses, x-ray and laboratory technicians to be trained in the most modern methods of fighting tuberculosis with a view to strengthening and expanding tuberculosis control services throughout Turkey.

W.H.O. EXPERTS RECOMMEND MEASURES IN WORLD-WIDE SHORTAGE OF NURSES

(SEA/PR/50-14, dated New Delhi, 8th March, 1950)

MEASURES to combat the world-wide shortage of nurses, and to improve their economic and social status were recommended by an Expert Committee of the World Health Organization which met in Geneva from 20th to 26th February, 1950. The Committee which was attended by members from eight countries, including Miss T. K. Adranvala, Chief Nursing Superintendent of the Directorate-General of Health Services of the Government of India, outlined proposals for raising the educational standards for nurses and auxiliary personnel in the light of recent advances in public health and medicine.

As things stand now the shortage of nurses is world wide, the Committee noted. 'The quantity of available nursing services', their report states, 'varies among nations from those with none whatever for millions of people, to those with one nurse for approximately each 400 persons. Illustrating this situation, it was mentioned that in England and Wales there were 5,000 beds available for the treatment of tuberculosis which remained empty owing to the lack of trained nursing personnel. In India only 100 to 200 nurses are employed in anti-tuberculosis work, whereas the actual needs of this country are estimated at 10,000 nurses in this one field.

As a first measure toward increasing the number of candidates for the nursing profession, the Committee recommended that studies be made, on the national as well as on the international level, of the factors preventing their recruitment. Since these factors are directly related to the social and economic status of women and to psychological attitudes of related health personnel and other population groups, the Committee recommended that these studies should be conducted by a staff including psychologists and sociologists.

In addition to these comprehensive investigations it was proposed that a joint W.H.O./ILO pilot study be undertaken on the working conditions of nursing personnel, including hours, salaries, health conditions and other personnel policies.

As far as standards of training are concerned, the Committee formulated a series of recommendations setting minimum requirements at all levels for nursing personnel, ranging from auxiliaries such as vaccinators to highly placed administrators of nursing services and specialized personnel in such fields as psychiatry and industry. These suggestions are intended for the use of the development of their nursing school programmes.

W.H.O.'s rôle in this field, the Committee stated, should be to provide governments with all information needed on various aspects of nursing, including the available training programmes throughout the world. Further it should foster educational opportunities through fellowships, sponsor international seminars on nursing problems, and promote a wide distribution of nursing literature everywhere. The International Council of Nurses was asked to co-operate closely with W.H.O. in this undertaking.

DRUGS RULES, 1945

No. F.1-2/47-D., Government of India, Ministry of Health, New Delhi, the 13th February, 1950

NOTIFICATION

In exercise of the powers conferred by section 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said section, namely :—

In Schedule K to the said Rules, after item 2, the following item shall be inserted, namely :—

'2A. Quinine and other anti-malarial drugs. Persons selling the drugs by retail under arrangements made by State Governments for sale and distribution of the drugs will be exempted from the requirement to take out licences for retail sale under clause (c) of section 18 of the Act.'

(Sd.) J. N. SAKSENA,
Under Secretary.

No. F.1-50/47-D., Government of India, Ministry of Health, New Delhi, the 28th February, 1950

NOTIFICATION

In exercise of the powers conferred by section 12 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said section, namely :—

To sub-rule (1) of Rule 25 of the said Rules, the following provisos shall be added, namely :—

'Provided that the drugs or classes of drugs are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit;

Provided further that if a single manufacturer has two or more factories situated in different places manufacturing the same or different drugs a separate licence shall be required in respect of the drugs manufactured by each such factory.'

(Sd.) J. N. SAKSENA,
Under Secretary.

No. F.1-31/47D., Government of India, Ministry of Health, New Delhi, the 13th March, 1950

NOTIFICATION

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely :—

In clause (9) of Rule 65 of the said Rules, after the word and letter 'Schedule H', the words 'and preparations containing such substances' shall be inserted.

(Sd.) J. N. SAKSENA,
Under Secretary.

MINUTES OF THE MEETING OF THE UNITED PROVINCES MEDICAL COUNCIL, HELD AT LUCKNOW ON TUESDAY, 20TH NOVEMBER, 1949

PRESENT :

Dr. A. C. Banerjee, M.B., B.S., D.F.P.H. *President.*

Dr. Abdus Samad, D.A., M.B.

Dr. A. Mundle, M.B., B.S., D.C.H.

Dr. Muhammad Abdul Hameed,
M.B., M.R.C.P.

Dr. Rameshwar Singh, L.M.S.

Dr. Prem Shanker Verma, L.M.P.

Dr. Ram Narain Lal, L.M.P.

Dr. Chaudhri Hardeo Singh Verma,
L.M.P.

Dr. S. P. Gupta, M.B., B.S.

Dr. R. N. Shukla, M.B., B.S.

Members.

*Registrar-
Secretary.*

1. The minutes of the last meeting were confirmed.
2. Government notifications nominating Drs. Gauri Shankar Bhargava, M.B., B.S., and Hari Nandan Bhatt, F.A.C.S., as members were read and recorded.
3. The statement of income and expenditure for the year 1948-49 was noted and sanction was accorded to excess expenditure, over the budgeted allotments, under certain heads.
4. The budget estimates for the year 1950-51, and the revised budget for the year 1949-50 were passed unanimously and it was suggested that the rates of registration fees charged in other provinces should be enquired and laid before the Council.
5. The postponed case against Dr. Ram Raghubir Bharadwaj, L.S.M.F., was considered and it was decided that there was no case against Dr. Bharadwaj.
6. The case against Dr. Damodar Singh, L.S.M.F., was considered and it was decided that the railway authorities should be called to appear before the Council, with necessary documents, to substantiate their complaint. Dr. Damodar Singh should also appear before the Council to establish his defence.
7. The case against Dr. Prafulla Kumar Bose, L.M.P., was considered and, after hearing Dr. Bose, it was decided that there was no case against him.
8. The recommendations of the Standing Committee, dated 28th November, 1949, were approved with slight modifications.
9. The sitting members of the Standing Committee were unanimously re-elected for 1950.
10. It was decided that the views or decisions of other Provincial Medical Councils regarding Common Seal for all Medical Councils should first be ascertained and specimen of their seals be obtained.
11. The request of Dr. Indira Narain Saksena, L.M.P., for restoration of his name to the medical register was postponed for consideration at the next meeting.
- 12 and 13. Withdrawn.

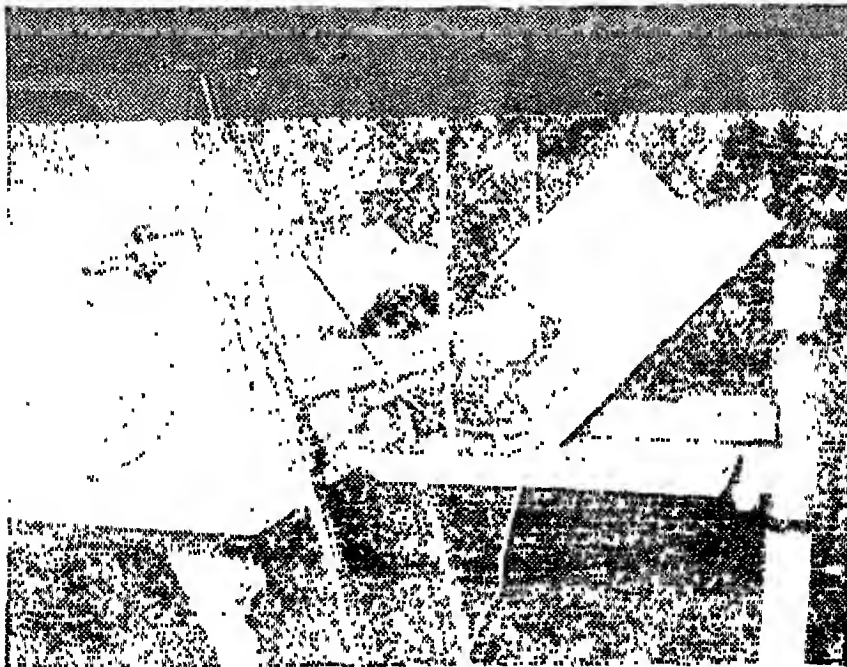
A. C. BANERJEE,
*President, Medical Council,
United Provinces.*

R. N. SHUKLA,
Registrar.



NEW DESIGN AMBULANCE PLANE

A new British air ambulance is being developed particularly for 'Bush' doctors in Australia and for medical men whose patients live in isolated areas. It is the Auster Avis Mk.2. As an air ambulance, provision is made to enable blood transfusions to be given while in flight. The plane will carry a standard full size stretcher and, apart from the pilot, has accommodation for a sitting casualty and an attendant. If the aircraft is not required as an ambulance it takes but a few moments to fit the necessary seats to convert the aircraft into a four seater. The Auster Avis Mk 2 air ambulance, showing how the side can be lowered to load a stretcher case.



LONDON RED CROSS EXHIBITION

At the Red Cross Society Exhibition held recently at Albemarle Street, London, a Red Cross worker, in the 'Iron Lung', demonstrates a new primatic Book Reader and a new automatic method of page turning, which she operates with her chin.



GYMNASIUM AIDS HOSPITAL PATIENTS

Rowing and cycling machines and other gymnasium equipment are being used to aid South London hospital patients to recovery. The gymnasium has been set up at St. Olave's Hospital, Rotherhithe, and it represents the first stage of a scheme started by Bemondsey and Southwark Hospital Management Committee. Patients in the gymnasium learn to use weakened muscles, through rowing and cycling machines, as well as other instruments.



FEATHERLIGHT HOSPITAL BED

A new type hospital bed to be shown at this year's B.I.F. (Earls' Court Section) is the 'Magbed'. Made of Magnesium Alloy it is featherlight and tremendously strong. Claimed as the greatest contribution in recent years to easing the problems of a ward staffing and fatigue of hospital personnel, it does away with the need for piles of pillows and bed blocks, and it is also designed to transport a patient from one hospital department to another without the necessity of transferring the patient to a conventional trolley. Its metal frame and smooth hygienic lines make it suitable for use in every climate in the world. The firm have received enquiries from India, Pakistan and Ceylon, as well as most of the other countries of Asia, Europe and America. (Manufacturers:—Essex Acro Ltd., The Airport, Gravesend, Kent, England.)



MOST MODERN PHYSICAL MEDICINE DEPARTMENT

A department of physical medicine, one of the finest in Britain, has been opened at Middlesex Hospital, London. Built on a bomb site adjoining the hospital, it possesses the latest equipment for all branches of physiotherapy including remedial exercises, electrical treatment, and artificial sunlight. Under the same roof is one of the largest physiotherapy teaching schools in Britain. Short-wave treatment being applied to the feet.

QUARANTINE RESTRICTIONS

(From a Release dated 6th April, 1950, issued by Press Information Bureau, Government of India)

Information has been received by the Director-General of Health Services that the Government of Afghanistan have issued a circular to their Embassies informing them that no visa is to be granted to any person who is not in possession of the necessary certificates stating that he has received inoculation, vaccination, etc., against contagious diseases.

In order to avoid delay and inconvenience on entry into Afghanistan, passengers leaving for that country are advised to be in possession of valid smallpox vaccination and cholera inoculation certificates. These certificates should be on the international form, signed or countersigned by a Medical Officer in Government or Municipal service.

THE 11TH MAHARASTRA AND KARNATAK PROVINCIAL MEDICAL CONFERENCE. DHARWAR. 6TH, 7TH AND 8TH OF MAY, 1950

THE 11th session of the Maharashtra and Karnatak Provincial Medical Conference is going to be held in Dharwar on 6th, 7th and 8th of May, 1950, under the presidentship of Dr. M. S. Wagale, L.M. & S. of Gadag.

R. A. Jahagirdar, Esq., M.A., LL.B., Vice-Chancellor, Karnatak University, Dharwar, has kindly consented to inaugurate the Conference.

Fees for the membership of the Reception Committee are Rs. 15 and for the Delegates are Rs. 5 for members and Rs. 6 for non-members of the Indian Medical Association.

Boarding and Lodging arrangements for Delegates are made in the Hostels of the Training College for Men and of the Karnatak College, Dharwar. A few separate rooms are reserved for Delegates coming with family. The Boarding charges are Rs. 15 for three days per head. Those who wish to attend the Conference should intimate the General Secretary of the Conference before the 25th of April, 1950.

DRS. R. V. Sathe, M.D., M.R.C.P., V. N. Shirodhor, M.D., M.R.C.S., B. D. Patwardhan, M.D. (Bom.), S. G. Joshi, M.S., and R. H. Karmarkar, F.R.C.S., etc., have agreed to speak on various subjects.

An Exhibition is also being arranged and we have received already a large number of applications for reserving the stalls. As the accommodation is limited, those who wish to take part in the Exhibition should intimate the Secretary of the Exhibition Committee of the Conference before the 25th of April, 1950.

For the benefit of the Delegates, Variety Entertainments are arranged at night on all the days.

On the whole, the Conference promises to be a success and it is hoped that Delegates from Maharashtra and Karnatak will attend the Conference in large numbers.

(Sd.) K. S. KAMALAPUR,
(Sd.) B. H. KAMALAPUR,
Hon. Secretaries.

THE WORLD MEDICAL ASSOCIATION

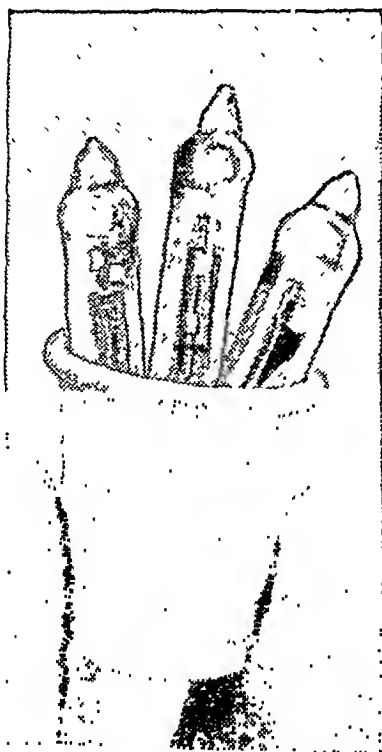
(Abstracts from Reports. *The Medical Officer*, No. 2152, Vol. LXXXII, No. 17, Saturday, 22nd October, 1949, page 175)

THE W.M.A. has successfully completed its recent sessions in London under the presidency of Dr. Charles Hill. This association, an international grouping of

national associations, is a purely voluntary effort and directly has nothing to do with W.H.O. though indirectly it was the outcome of it. Twenty-four nations, each of which has its own medical association, have joined W.M.A. and it is expected that all will join it eventually. The oldest medical association is our own B.M.A., which is the pattern upon which most other national medical associations were built.

The objects of W.M.A. are the same as those of the B.M.A. to promote the science and art of medicine and to guard the interests of patients and practitioners. At the meeting of the W.M.A. in Geneva last year, 12 principles regulating medical practice were laid down, but these are tentative and open to several objections on the grounds of impracticability on an international scale.

There is undoubtedly the desire of all medical associations for unity of aim and a common basis of practice, but the influence of national laws and customs makes these obtainable only in limited degrees. Yet the W.M.A. can be a body of considerable power, though much will depend upon the personalities of the representatives.



NEW SUB-MINIATURE VALVES

These sub-miniature valves, developed for hearing-aid sets by a British firm, are the smallest of their class in the world. Their smallness can be gauged from the fact that they are one-fortieth the size of an average radio receiving valve. They are made by Mullard Ltd., of Shaftesbury Avenue, London, who made 400,000 sub-miniature valves for the National Health hearing-aid in 1947. The experience gained by the firm's scientists and craftsmen on this led to the development of the new DF66 and DI66 valves. This picture shows three DF66 valves in a thimble.

W.H.O. IN THE FIELD : WIDESPREAD SERVICES IN OPERATION

(Abstracts from Reports, W.H.O. Newsletter, World Health Organization, No. 10, September 1949)

W.H.O. has sent three malaria teams to India and will soon send a fourth. These teams, using materials supplied by UNICEF and co-operating with Indian personnel, will demonstrate the technique of malaria control in selected areas over a period of two years increasing the size of the area each year and expanding the local malaria organization so that the ever-widening area of control measures can be continued by local personnel after the withdrawal of the W.H.O. team.

One team at Terai in North Central India is headed by a Greek malariologist. The second team headed by a Canadian malariologist will work in the Jaspore Hills in Central Eastern India. A third team headed by an American malaria engineer is working in Malnad on the western border of Mysore in South West India and the fourth team, when it is formed, will work in Wynad in the same province. The operations in each one of these areas will protect about seventy-five thousand people in the first year. In the second year, the area will be doubled and so on until malaria control is applied to all infected areas within the country.

Other areas in Asia will also benefit from the programme. A team is already in East Pakistan at Gomripur, north of Dacca, carrying out exactly the same plan for the demonstration of techniques, organization methods and training of personnel, and another team is in position in Chiangmai in the Serapee District of Northern Thailand. In Afghanistan a survey team is selecting a suitable area for a demonstration project.

THE DUTCH ARCHIVES OF SURGERY

(*Archivum Chirurgicum Neerlandicum*)

(New Official Organ of the Dutch College for the Advancement of Surgical Science, including the Dutch Societies for General Surgery, Orthopaedic Surgery, Urology, Neuro-Surgery, Plastic Surgery, Thoracic Surgery and Anaesthesiology)

This new quarterly is published in English (with a very occasional article in French or German) under the direction of the distinguished editorial board named on page three of this announcement and includes articles first written in Dutch, German, French or English. The first number is now available. Subscription rate in the British Empire is £2-2-0 per year. Published by S. Gouda Quint-D. Brouwer En Zoon Arnhem, The Netherlands. Sole Agents for the British Empire: Baillière, Tindall and Cox, 7/8, Henrietta Street, London, W.C.2.

CONTENTS OF THE FIRST NUMBER :

Foreword.

By Dr. I. Boerema, Editor in Chief, Professor of Surgery in the University of Amsterdam, President of the Dutch College for the Advancement of Surgical Science.

Pericardectomy for Constrictive Pericarditis.

By Dr. L. D. Eerland, Professor of Surgery in the State University of Groningen.

Surgical Treatment of Carcinoma of the Distal Three Quarters of the Thoracic Oesophagus and the Cardia.

By Dr. J. F. Nuboer, Professor of Surgery in the State University of Utrecht.

'Androgen Control'—Therapy in Cases of Cancer of the Prostate.

By Dr. H. Muller, Assistant in the Surgical Department of the State University of Leiden.

Retropublic Prostatectomy by T. Millin.

By Dr. J. A. Weytlandt, Urologist, Amsterdam, Secretary of the Dutch Society for Urology.

A Case of Aneurism of the Aorta after Resection for Coarctation, Cured by Excision.

By Dr. J. R. Blickman, Assistant in the Surgical Department of the University of Amsterdam.

Operative Treatment of Severe Kyphosis as the Result of Bechterew's Disease.

By Dr. G. Chapchal, Head of the Orthopaedic Department of the State University Surgical Clinic of Utrecht.

Primary Enterococcic Peritonitis.

By Dr. J. Kweekel, Chief Assistant in the Surgical Department of the State University of Leiden.

Pneumectomy in a Case of Besnier-Boeck's Sarcoidosis.

By C. L. Peterson, B.A., M.D., Assistant in the Surgical Department of the University of Amsterdam.

CONTENTS OF THE SECOND NUMBER :

L. D. Eerland : Estragenital (?) Chorion-epithelioma in the Male in the Appearance of a Primary Lung Tumour (91).

J. Glazenburg : The Chronic Undermining and Burrowing Ulcer of Meleney (99).

M. J. Kingma : Hæmolytic Streptococcus Gangrene of the Skin (110).

R. Brummelkamp and C. H. Veerboek : Congenital Cyst in the Common Bile Duct in a New-Born Infant (113).

A. Nijland : Coelomic Cysts (121).

M. P. A. M. De Grood : Indications, Technique and Results of the Torkildsen Ventriculo-cisternostomy (130).

L. D. Eerland : Thoracotomy and Extirpation of Mediastinal Metastases after Sarcoma Tibiæ Sinistræ (138).

R. Brummelkamp : The Influence of the Gastric Acidity on the Genesis of Gastric Ulcer (143).

A. C. De Vet : Plastic Repair of Skull Defects with Acrylic Plates (153).

A. J. Eijkman : A New Guide Apparatus for Drilling the Guide Wire in the Operative Treatment of Fracture of the Femoral Neck (163).

OUTBREAK OF Q FEVER IN LONDON

(Abstracted from *The Medical Officer*, No. 2147, Vol. LXXXII, No. 12, Saturday, 17th September, 1949, page 122)

ON 11th, 12th and 13th July, three members of the pathological staff and one nurse at a London hospital became ill with what appeared to be atypical pneumonia. All recovered, but subsequent investigation has shown that all now have significantly high agglutinations against rickettsia burneti. The rickettsia has also been recovered from one sample of blood. The usual incubation period (10-24 days) has now expired and there is no evidence of further spread of the disease in the hospital. The source of infection is being investigated.

This is believed to be the first occasion upon which rickettsia burneti has been recovered in this country.

Q fever was first distinguished as a human disease in Queensland, Australia, in 1935, and was thought to be tick borne.

The occurrence of this small outbreak in England, where there is no evidence of endemicity, is particularly noteworthy. Although the present episode may be no more than an isolated importation, it calls for special vigilance. Early recognition of the disease and the correction of any environmental factor likely to facilitate spread may prevent the establishment of endemicity.

CLINICAL FEATURES OF Q FEVER

Q fever is an acute febrile disease closely simulating virus pneumonia. It is not easily differentiated from influenza, primary atypical pneumonia, psittacosis, and other obscure fevers. The disease is characterized by sudden onset which can be dated, headache (commonly frontal, behind the eyes), weakness, sweating and chills, and body aches. Pleuritic pain and cough frequently occurs and the sputum may be blood stained, although expectoration is as a rule scanty. As in virus pneumonia, physical signs of pulmonary involvement are relatively slight compared with the radiological findings which are, generally speaking, indistinguishable from primary atypical pneumonia. The white count is normal or decreased, with a relevant lymphocytosis. Fever is usually high and persists from one to ten days or more; in most cases it is of from three to six days' duration. Anorexia may be pronounced at the onset and the fever may be very debilitating.

Q fever is distinguished from the other rickettsial diseases (epidemic typhus, scrub typhus, Rocky mountain spotted fever, rickettsiapox) by the rarity of cutaneous lesions. A fine vesicular eruption of short duration may occur in less than 10 per cent of cases. In this rickettsiosis the Weil-Felix reaction is negative.

[See Editorial, *I.M.G.*, Vol. 84, p. 57.—Editor, *I.M.G.*]

MALARIA CONTROL IN THE BRITISH COLONIES

THIS pamphlet, issued by the Central Office of Information, London, contains an account of the discoveries of the pioneers in anti-malaria work, recent advances in the use of drugs and insecticides and some of the method now employed to combat malaria in the British Colonies. It should be useful for the purpose of reference.

**FIFTH SESSION OF W.H.O. EXECUTIVE BOARD.
REPORT ON S.-E. ASIA HEALTH PROBLEMS**

(Reproduced from Press Release SEA/PR/50-5, dated New Delhi, 30th January, 1950, issued by World Health Organization Regional Office for S.-E. Asia)

At a meeting held late last week the Fifth Session of the W.H.O. Executive Board in Geneva reviewed the work of the Regional Organizations of W.H.O., and warmly praised the rapid progress which had been made in the development of health activities in South-East Asia and the Eastern Mediterranean.

The tremendous health problems of the 400 million population of the S.-E. Asia area were outlined in a report on the work of the S.-E. Asia Regional Committee which was introduced by Dr. C. Mani, Regional Director. 'Shocking poverty' and high death rates among all groups, especially infants and mothers, were singled out by the report.

Malaria, responsible for 100 million cases and 1 million deaths yearly, was closely followed in importance, according to the report, by tuberculosis

and pestilential diseases, while leprosy and filariasis were also grave problems.

It was stated that public health administrations in the region were underdeveloped. They were often manned by competent staff, but few in numbers and hampered by lack of medical supplies and equipment.

The aim of W.H.O. in the region, it was stated, was first to build up national health administrations by organizing training facilities and disease control projects, and by providing fellowships. A programme on these lines was already underway in the S.-E. Asia region.

The co-operation of the U.N. Economic Commission for Asia and the Far East (ECAFE) must, according to the Executive Board, be sought to encourage the production of medical supplies.

Dr. Mani described the unfavourable effects of the recent currency devaluations on national health budgets in S.-E. Asia. The countries of the region, he said, had agreed on a policy of mutual help on a multilateral basis to develop local production of DDT, sulphanilamides, penicillin and other essential drugs.

Dr. Brock Chisholm, W.H.O. Director-General, commented upon the remarkable degree of collaboration achieved in all regions, and added that all developments pointed to a decentralization policy as being the 'healthiest way' for W.H.O.

Dr. Mani was congratulated by the Chairman and several members of the Board.

W.H.O. BOARD URGES DEVELOPMENT OF REGIONAL HEALTH ACTIVITIES

(Reproduced from Press Release SEA/PR/50-6, dated New Delhi, 1st February, 1950, issued by World Health Organization Regional Office for S.-E. Asia)

BROAD development of the World Health Organization's regional activities has been urged by the W.H.O. Executive Board in Geneva after a two-day discussion of general long-range organization policy.

Sir Arcot Mudaliar (India), Chairman of the Board, summarizing comments by the speakers, declared that W.H.O. in a few years should develop into an organization carrying on from Headquarters only certain essential tasks and delegating all operational responsibilities to regional offices.

Tasks assigned to Headquarters, he said, should be those such as biological standardization, which would continue for years along lines fixed in advance. Disease control plans, on the other hand, should be carried out entirely on a regional level and reviewed periodically by regional committees with guidance by the Assembly, he continued.

The Board considered that Headquarters' activities should include development of a system for collection and dissemination of epidemiological data; adoption of international nomenclature; development of further standards for biologicals, pharmaceuticals, dietetics and laboratory tests; unification of pharmacopoeias; and development of technical education to help overcome a general lack of adequately trained auxiliary personnel.

Discussing the programme of work for four years, 1952-1956, the Board agreed unanimously that it was imperative to increase regionalization of a substantial portion of work. General plans, as drawn up by Health Assemblies, must be adapted to local needs and conditions, the Board observed, and such action could best be taken by regional organizations themselves.

Various members pointed to the need for regional bodies to develop a great degree of self-reliance and suggested that regional organizations need not rely

solely on the W.H.O. budget but also should mobilize resources within the region.

The first of W.H.O.'s regional organizations was set up in S.-E. Asia at the end of 1948 with Headquarters in New Delhi. Earlier, the Executive Board had expressed satisfaction with a report presented by Dr. C. Mani, W.H.O. Regional Director for S.-E. Asia, on the work already accomplished. The S.-E. Asia region includes Afghanistan, Burma, Ceylon, India, and Thailand.

The Indian Medical Gazette Fifty Years Ago

RECENT ITALIAN WORK ON MOSQUITO MALARIA

(From the *Indian Medical Gazette*, March 1900,
Vol. 35, p. 101)

WE are glad to see that in their recent communication to the Tenth Congress of the Italian Society of Internal Medicine, Drs. G. Bastianelli and A. Bignami take a more liberal view of their indebtedness to previous observers and more especially to the work of Ronald Ross than they seem inclined to do when their earlier work on Mosquito Malaria was published. We are indebted to the *Lancet* (January 13th) for a translation of a very valuable article by these authors. We will here endeavour to give a summary of this article, as it touches upon many points of extreme interest to all who wish to understand what is claimed for what is called the mosquito theory of malaria. The writers begin by referring to the two mosquito theories, *viz*, that which they attribute to Manson, that is that the mosquito sucks the malarial blood and then dies in water, and so infects the water, just as the mosquito does in the case of elephantiasis. This theory was only provisionally put forward by Manson, and it is by no means certain that direct injection by the mosquito is the sole way that the infection can be conveyed. Manson, however, in common with nearly all other writers, now adopts the view that primary malaria is usually conveyed into the human system by the direct bites of the mosquito, as Ross has proved in the case of the proteosoma of birds, and as Bignami in his former article attempted to prove for man. It was Grassi who pronounced as 'suspected' all the species of mosquitoes which are found in malarial localities and are not found in healthy ones, *viz*, anopheles claviger, culex pencillar, and the so-called culex malarie. It was with these species captured in the adult state in 1898 that the first case in man of experimental infection of malaria was obtained, though it could not then be decided which species was responsible. Subsequent researches showed that it is the genus anopheles which is the extracorporeal

host of the malarial parasite. Our authors give a resume of the cycles of the aestivo-autumnal parasites, which they claim to have traced from the blood of a malarial patient to the salivary gland of the mosquito 'in perfect accordance with that described by Ross in the cases of the proteosoma of birds in the grey mosquito'. They then show that the same facts hold good for the tertian and quartan parasites. 'All three species of malarial parasites, distinguishable with certainty from each other, adopt as host the same species of mosquito'. They have seen with Grassi that anopheles, after having sucked blood containing crescents, on subsequently biting a healthy person communicated to him the aestivo-autumnal infection; and recently they have made a corresponding test with tertian parasites, showing that anopheles, after having bitten a tertian patient, become capable of inoculating tertian fever into a healthy patient. It is also shown that it is not possible to transform the tertian parasite into the aestivo-autumnal by the agency of a higher summer temperature.

So that even after their passage through the anopheles the species of malarial parasites remain distinct and do not become transformed one into the other. 'Besides this result our inoculation experiments permit us to affirm that a single infected mosquito is capable of inoculating malaria into man'. This is an observation which, if confirmed, is of the greatest practical importance. But our authors go further, namely, 'that a single mosquito by successive bites can infect several people; in fact, on examining some of the mosquitoes employed in our experiments after they had bitten the healthy subject, who had subsequently taken the fever, we have still found sporozoites in the salivary glands and mature capsules with sporozoites in the intestine, proving that even if at a single bite the anopheles empties all the contents of its salivary glands, the glands may still become affected afresh. And more than this, since it may occur that the two species of parasite may develop in one and the same mosquito, for instance an aestival and a tertian, the two, as we have proved, remaining distinct, it may well happen that a single anopheles may inoculate a mixed infection, e.g. aestival and tertian'. Indeed it is well known that mixed infections of aestival and tertian are by no means rare in Italy. Our authors next proceed to discuss the practical bearings of the knowledge that the malaria parasites have two necessary hosts. Thus, to explain completely the course of a malarial outbreak, it is necessary to study, firstly, the malarial individuals, secondly, the malarial mosquitoes, and thirdly, the places in which the larvæ of the anopheles develop, that is the 'malarial soil' in the traditional sense of the expression. Our authors made such a study at the well-known malarious locality of Ostia in the spring and summer of

1899. With regard to the malarial patients it was found that as a rule in winter only relapses of aestival tertian and quartan are found. As the season advances the relapses of aestival become more and more rare until in the spring it is most difficult to find a patient with crescents. On the other hand, relapses of tertian and quartan continue to occur right through the spring up to the commencement of the new malarial season, which begins in the first week of July with a sudden increase in the number of patients. During the spring some rare cases of first attack of common tertian are met with, but the fact remains that the malarial season proper, with its fresh outbreak of primary attacks, does not commence till the beginning of July and does not terminate till the end of the autumn. This holds good for all varieties of malaria. So far so good, but it is not easy to see how our authors decide upon what is a 'relapse' and what is a 'new infection'. In fact they admit this in the next sentence, when they remark 'patients who had suffered from fever in the previous year, in whom it was not possible to be certain whether we had to do with a relapse or a reinfection'. So much for the malarial patients, the writers now turn to the observations made at the same time on the anopheles. In Ostia it is the anopheles claviger which almost exclusively prevails. In the months of March, April and May, anopheles were found in the houses, in the stables, and also under the bridges, generally with mature ova.

In the month of June anopheles began to be found infected with the parasites, but only those caught near inhabited places, which probably had taken the parasite from persons suffering from relapses. It was also found that wherever the people gathered together, there the infected anopheles began to be found in abundance. The following figures are very instructive. Of the anopheles collected in the huts of seven people on 1st July, only two out of seven were found to be infected; of those collected on 9th and 10th July, two out of seventeen; of those captured on the 17th, fifteen out of thirty-two; on 20th July the number of infected anopheles rose to eleven in seventeen, or about 64 per cent, some of them presenting ruptured capsules and mature sporozoites while of those captured in the stables or in places remote from human habitations none were found infected. By the end of July nearly all the men who had slept in these huts were affected with either the aestival or with tertian fever. The progressively increasing number of anopheles affected explains in the clearest manner the final outbreak of fever among all the labourers.

It would thus appear from the above observations that the outbreak of malaria in its severe form in July can be explained by the presence of anopheles which had become infected by the cases of fever relapses which were met with in May and June.

Dr. Bignami goes on to describe his study of the localities in which he found the anopheles develop, and this portion is not only interesting but of great practical importance. It shows moreover that what is true for the anopheles in Sierra Leone is not necessarily true for other localities, as observers in India have already begun to find. The district of Ostia is intersected by drainage canals which collect the water of the lowest levels and convey it to the elevating machines by which it is emptied into the sea. Now in all the secondary canals and in that part of the main canal furthest from the elevating machines, where there grows a rich vegetation of reeds and algae, there was found an immense number of larvae of the anopheles. The larvae were absent from the water of the canals near the machines where the current was strong, everywhere else where the current was slack or where it tended to stagnate the development of the larvae was most vigorous. Another favourite breeding place was in a small lake on the estate of Castel Fusano. This observation, we think, is of great importance to us in India. We all know how an increase of fever in many places has been popularly attributed to the increase of irrigation. We may remember how the origin of the great Lower Bengal fever epidemic of the seventies has been attributed to the bunding up of a river in the Jessore district. It may well be that the real cause is that the water-logged condition of such areas affords numerous breeding places for the anopheles. These observations, although only meant to apply to the district of Ostia in Italy, also suggest to us the possibility that if similar localities in India were examined, we might have similar results. At any rate it is clear that we must not confine our attention to small puddles only in the search for the anopheles, as a too literal following of the reports of Major Ross's expedition has led many to do. The peculiar habitat and breeding place of the anopheles must be discovered in every place in which it is proposed to attempt the extirpation of the peccant mosquito.

It is also to be noted that while we, in the British Empire, are attempting to banish malaria, by banishing the extracorporeal host of the parasite in other countries, this is not being attempted. Koch has already announced that the way to get rid of malaria is to kill the parasite while still in the patient's blood, and in this article Dr. Bastianelli and Bignami preach the same doctrine. They write: 'The careful treatment of the individual patient constitutes one of the principle tasks of hygiene . . . energetic treatment by quinine, from the commencement of the infection, of the aestival fevers not only reduces the dangers of relapses to a minimum, but has evidently a great importance for general prophylaxis, since the parasites by this means could be prevented from developing

into those forms which continue their life in the anopheles'. Here also we have a justification for our practice of attempting to limit the ravages of malaria by what is known as the prophylactic issue of quinine.

There are, therefore, the two methods of attempting to banish malaria, which we may call the British and the Continental; which will turn out to be the most practical remains to be seen, for our own part we think it a counsel of perfection to tell us to attempt to get rid of fevers in a country like India by means of dosing the people with quinine. By all means let us do all we can to inculcate a belief in the virtues of quinine, and to encourage its use. We would also enter a plea for the more thorough treatment of individual cases of malarial fever; we should not be content to leave off the quinine because the fever has disappeared—disappearance of fever by no means implies the destruction of the parasite.

This may be granted, yet we think there is more hope in the British method; it is difficult to get rid of every spot where the anopheles might flourish, but at least it is less chimerical to hope for than the thorough dosage with quinine of every man, woman and child who may have suffered from fever during a fever season. And moreover we must remember that it was probably by destroying the haunts of the anopheles that malaria has been banished from well-drained and well-cultivated countries in which it formerly held sway.

Current Topics, Etc.

Continuous Intravenous Injection of Typhoid Vaccine in Treatment of Certain Ophthalmic Diseases

(Reproduced from Medical Newsletter No. Wa 216, January 1950, prepared by the American Medical Association)

CURRY AND SHAW point out that for many years artificial fever, induced in a hypertherm cabinet or by injections of foreign protein or typhoid vaccine, has been used in the treatment of various diseases of the eye. Attention has been directed particularly toward the use of single, rapid intravenous injections of typhoid vaccine. A drawback of this type of therapy is the unpredictable febrile reaction. Moreover, typhoid therapy is frequently withheld from elderly patients or persons with heart disease because of the risk entailed in a severe reaction. Solomon and Somkin in 1942 introduced the method of controlled hyperpyrexia by the continuous intravenous administration of typhoid vaccine. It occurred to the authors that this type of therapy might well be applied to the treatment of certain ophthalmic diseases.

One cubic centimetre of typhoid vaccine in a concentration of 1,000,000,000 killed organisms per cubic centimetre was suspended in 1 litre of sterile isotonic

sodium chloride solution U.S.P. With the patient in bed, a 21-gauge intravenous needle was inserted in an antecubital vein and the mixture allowed to flow at a rate of 20 to 30 drops per minute. Rectal temperatures were recorded at fifteen-minute intervals. If the temperature did not begin to rise in 30 to 45 minutes, the rate of flow was doubled. If the rise in temperature was rapid, the rate of flow was decreased. The degree of fever desired varied from case to case, depending on the condition under treatment and the physical condition of the patient.

Summarizing their experience with this method the authors say that a total of 17 patients with ophthalmic diseases, including non-specific iritis, syphilitic keratitis and suspected sympathetic ophthalmia, were treated by the continuous intravenous administration of typhoid vaccine, with gratifying results in every case. This method of treatment is recommended because it may be given safely to elderly and debilitated patients and the degree of fever and chilling may be controlled.

(Curry, J. J., and Shaw, E. A.: *Archives of Ophthalmology*, 42, 123-125, August 1949. The authors are connected with the Robert Dawson Evans Memorial and the Ophthalmologic Service, Massachusetts Memorial Hospitals, Boston, Mass.)

Cure of Chronic Vivax Malaria with Pentaquine

By L. T. COGGESHALL
and
F. A. RICE

(Abstracted from the *Journal of the American Medical Association*, Vol. 139, 12th February, 1949, p. 437)

PENTAQUINE, 30 mg. daily, and quinine 2.0 gm. daily, later reduced to 1.0 gm. daily, taken simultaneously for fourteen days, have resulted in the termination of relapsing vivax malaria in 163 of 185 infected ex-servicemen, although the majority were experiencing relapses every four to six weeks prior to treatment.

The therapeutic regimen was an ambulatory one and did not require interruption of normal activities.

Toxic reactions encountered were not sufficient to cause concern and were largely those commonly associated with the use of quinine.

Ewing's Tumour

(The following two items are reproduced from *Surgical Newsletter* No. Wa 219, January 1950, prepared by the American Medical Association)

THE purpose of this report by McSwain and associates is primarily to report the apparent cures of three patients with Ewing's tumour of bone (in one of whom there was disappearance, without direct treatment of an apparent pulmonary metastasis), and secondarily to summarize the features of all cases of Ewing's tumour which have been seen at the Vanderbilt University Hospital since 1925. There have been 192 specimens of bone tumours, exclusive of metastases, submitted to the Surgical Pathology Laboratory, of which 71 were malignant. The 20 Ewing's tumours found in this series thus represent an incidence of 10 per cent of all bone tumours and 28 per cent of malignant bone tumours.

Thirteen of the 20 cases concerned males. The fact that Ewing's tumour is more frequent in males than in females has also been pointed out by other observers. The ages of the 20 patients varied between 3 and 43 years. It is rare for Ewing's tumour to occur in patients over 40 years of age.

The periods which had elapsed from the onset of symptoms until the application to this clinic for treat-

ment ranged from 5 weeks to 12 months, the average time having been five months for all patients and slightly less than five months for the individuals who died. The patients still alive had had symptoms for four and ten months, respectively. In ten patients there was no injury, while in each of the other ten there was a definite history of a severe injury; however in one patient injury occurred 25 years before admission.

Pain and swelling was noted in practically all instances. The authors found the tumours more frequently in flat bones (14 cases) than in long tubular bones (six cases). This contradicts the observations of Ewing, Geschickter and Copeland, but corroborates those of Stout, Lichtenstein and Jaffe.

In most instances, the tumours were visible and in all patients they were palpable. Most of the tumours were smooth and all of them were firm or hard, and immovable. None was fixed to the skin.

The roentgenologic findings in these patients were so variable that the diagnosis of Ewing's tumour was made by the roentgenologist in only five of the cases which occurred in the flat bones and in none of those which occurred in the long bones. The changes in two of the tumours of long bones were thought to be due to osteomyelitis. In one instance the so-called 'sunray' picture was seen and in another patient the characteristic roentgenologic findings of a bone cyst in the 12th rib were observed. In one instance in this clinic the fairly characteristic 'onionpeel' appearance has been seen in a bone lesion which on microscopic examination proved to be an osteogenic sarcoma.

The authors believe that it is impossible to make an unequivocal diagnosis of Ewing's tumour by means of the roentgenogram alone and that all such lesions should be subjected to exploration and removal of tissue for microscopic examination.

No suspected case of Ewing's tumour should be subjected to irradiation or amputation until microscopic examination of excised tissue has confirmed the diagnosis.

It has been possible apparently to cure this disease in one instance by amputation, in another by irradiation, and in a third instance by irradiation and amputation.

Two instances have been recorded in which, without direct treatment, apparent pulmonary metastases from Ewing's tumour disappeared. The following hypotheses have been considered to explain the disappearances of the pulmonary nodules: (1) They were not metastatic neoplasm. (2) They were so radiosensitive that the tiny amount of irradiation from the diagnostic chest roentgenography caused them to disappear. (3) Irradiation of the site of the primary tumour activated the cells in the circulation which rendered secondary irradiation to the lungs. (4) Irradiation of the gonads changed the hormonal balance in such a way as to establish conditions which were incompatible with life of the tumour cells. (5) So-called Ewing's tumour is not a neoplastic but an inflammatory disease.

(McSwain, B., Byrd, B. F., Jr., and Inman, W. O., Jr.: *Surgery, Gynecology and Obstetrics*, 89, 209-221, August 1949. The authors are connected with the Department of Surgery, Vanderbilt University School of Medicine, Nashville, Tenn.)

The Disc Syndrome: Results of the Conservative Care of Patients with Positive Myelograms

COLONNA AND FRIEDENBERG say that the rôle of the herniated disc in the picture of backache and radicular pain is controversial. Some clinicians believe that the disc accounts for a small fraction of such cases, while others believe that all back pain with radiation is encompassed within its limits. Widely divergent

views exist regarding operative indications, the extent of the operation to be done, and the question of whether or not spine fusion should follow disc removal.

At the Hospital of the University of Pennsylvania, almost all of the cases of low-back pain and radicular pain are treated by a period of conservative therapy, consisting of bed rest on a firm support, traction, adequate sedation, daily physical therapy and, when the patient is ambulatory, some form of back support. If the patient fails to respond to these measures within a few weeks, and if there is a history of repeated attacks of severe pain, a myelogram is indicated. If he is having an acute, intractable attack, and if there is definite myelographic evidence of a protruding mass, surgery is usually resorted to.

In each of the 28 patients studied by the authors, a clinical diagnosis of protruded nucleus pulposus was advanced. Such a diagnosis was usually based on a history of backache and radicular pain, associated with impaired spinal mobility, spasm of the erector muscles, positive straight-leg-raising test, and sciatic scoliosis. In addition, reflex sensory changes and atrophy of the lower limb were commonplace. Routine roentgenograms of the lumbar spine and pelvis were either negative or showed some intervertebral narrowing. Each patient was given an oil myelogram. A definite diagnosis of a protruding mass in the lumbar canal was noted under the fluoroscope and was confirmed by anteroposterior, oblique, and lateral views of the oil column. Patients with only air myelograms were excluded from this study because of the unreliability of this diagnostic medium.

The 28 patients in this study were followed from one to eight years after myelography, with an average follow-up of 2.7 years. All patients were treated with braces, restricted activity, and physical therapy following their hospitalization. Twenty lesions were in the fourth to fifth lumbar interspace, six in the fifth lumbar to first sacral interspace, and three in the third to fourth lumbar interspace. In one case the lesion was multiple.

Thirteen patients improved remarkably with bed rest and traction. In four, surgery was withheld, as this was the initial attack. In seven others, the surgeon felt that the pain at the time of examination was insufficient to warrant operation. Four patients refused surgery.

The results in this series are viewed in relation to material from a prior study in which 95 patients were examined one to five years after removal of the lumbar intervertebral disc.

In the non-operative group, eight patients (29 per cent) were in the pain-free category; in the operative group, 57 patients (60 per cent). Twenty (71 per cent) of the 28 patients had residual pain; whereas only 38 or 40 per cent were in this category in the operative group. Thus the results in this conservatively treated group compare unfavorably with the results obtained in a carefully selected operative series. The chronicity of this disease must be fully appreciated; most of these patients had suffered five years or more. There can be little justification for letting the disease run its course.

(Colonna, P. C., and Friedenber, Z. B.: *Journal of Bone and Joint Surgery*, 31-A, 614-618, July 1949. The authors are connected with the Department of Orthopaedic Surgery, Hospital of the University of Pennsylvania, Philadelphia.)

The Use in Children of Procaine Penicillin with Aluminium Monostearate

By J. L. EMERY *et al.*

(Abstracted from the *British Medical Journal*, i, 25th June, 1949, p. 1110)

Blood penicillin levels have been followed in 66 children of varying ages given graded doses of

procaine penicillin in arachis oil with 2 per cent aluminium stearate in which over 95 per cent of the particles were below 5μ in diameter.

The doses given were 75,000 units (0.25 ml.) and 150,000 units (0.5 ml.) to children under 1 year, 150,000 units to children aged 1-4 years, and 300,000 units (1 ml.) to older children.

There is a rapid initial absorption of penicillin, giving a level above $0.2 \mu\text{ml.}$ by the end of the first hour, and this level is maintained for at least three hours.

In all but one case a blood penicillin level of $0.06 \mu\text{ml.}$ or more was maintained for at least 48 hours after injection.

Children given daily and alternate daily injections maintain a continual penicillin level in the blood, the daily injection producing higher levels than the alternate daily injection.

The authors conclude that procaine penicillin in arachis oil with 2 per cent aluminium stearate is a suitable preparation for the daily injection of penicillin.

A Simple Weight-Reducing Diet

By H. L. MARRIOTT

(Abstracted from the *British Medical Journal*, ii, 2nd July, 1949, p. 18)

The essential instructions are as follows:

1. Eat or drink as much as you like (or can get) of:—

Lean meat, poultry, game, rabbit, hare, liver, kidney, heart, sweetbread—cooked in any way, but without addition of flour, breadcrumbs, or thick sauces.

Fish (not tinned), boiled or steamed only; no thick sauce.

Eggs, boiled or poached only.

Potatoes, boiled, steamed or baked in skins, but not fried, roast, sauté, or 'chips'; not potato powder.

Other vegetables of all kinds (fresh, tinned, or dried) cooked in any way not involving the use of fat.

Salad and tomatoes without oil or mayonnaise.

Beetroot, radishes, watercress, parsley.

Fresh fruit of any kind, including bananas. Also bottled fruit if bottled without sugar. Not tinned or dried fruits (including dates, figs, and raisins).

Sour pickles, not sweet pickles or chutneys.

Clear soup, broth, 'bovril', 'oxo', 'marmite'.

Salt, pepper, mustard, vinegar, Worcester sauce (no other sauces).

Saccharine for sweetening.

Water, soda-water, and non-sweetened mineral waters.

Tea and coffee (milk only as allowed below).

2. You may have milk (not condensed) up to half a pint (284 ml.) daily. No cream.

3. You may have three very small pieces of bread per day and take them either one at each main meal or all three at one meal as desired. 'Very small' means not exceeding 1 oz. (28 g.).

4. You may have *nothing else whatever*: particularly note that this means:—

No butter, margarine, fat or oil (except for cooking, not fish).

No sugar, jam, marmalade, honey, sweets, chocolate, cocoa.

No puddings, ices, dried or tinned fruits, nuts.

No bread (except as above), cake, biscuits, toast, patent reducing breads, cereals, oatmeal, 'all-bran', 'ryvita', 'vitawheat'.

No barley, rice, macaroni, spaghetti, semolina, sausages, cheese.

No cocktail savouries, alcohol (beer, cider, wines, and spirits).

Weigh before you begin, and thereafter weekly, on the same scales, in the same clothes, and at the same time of day.

The general principle of the diet is simply to allow unrestricted consumption of specified low- and moderate-calorie foods, with measurement of only two foods, milk and bread. It is therefore very simple, and patients generally report it as easy to carry out, even in these days, whether eating at home or in restaurants or as guests.

The opening words 'eat or drink as much as you like' seem to predispose to willing co-operation. Encouragement to eat unlimited potatoes generally occasions pleasant surprise. The lay public has deeply rooted the notion that potatoes are more fattening than anything else and, consequently, the obese have usually been denying themselves potatoes, which, in fact, are not of high calorie value unless covered and impregnated with fat in cooking. Obese subjects can eat liberal helpings of boiled, steamed or baked (without fat) potatoes three times a day and still continue to lose weight.

Weight lost by patients, who adhere faithfully to the diet without any lapses, varies from 15 to 35 lb. (6.8 to 15.9 kg.) in 12 weeks. More can be lost (up to 60 lb. (27.2 kg.) in the very fat) by going on. Prolonged experience enables one to say that a patient with simple obesity who does not lose weight is eating or drinking outside the permitted articles.

After weight reduction has been achieved the patient is left knowing the foods which are most fattening. He or she should be advised to return to ordinary diet but to maintain weekly weighing and check any observed tendency to regain weight by moderate restriction of consumption of the articles listed in Instruction 4.

Cortisone in the Treatment of Rheumatism

(Abstracted from the *British Medical Journal*, ii, 2nd July, 1949, p. 24)

THE discovery of the adrenal hormone compound E, by Dr. Edward C. Kendall, now named by him 'cortisone', and its application in the treatment of rheumatoid arthritis by Dr. Philip S. Hench and his colleagues, were recently discussed in a leading article in this journal.

The publicity which is naturally and rightly given to the almost unbelievable improvement obtained when cortisone is used to treat rheumatoid arthritis has raised the hopes of countless patients, who will no doubt want to know from their doctors whether they can gain similar benefit. Unfortunately, cortisone will not be available for very many months, except in small quantities to be used for further clinical trials under, it is hoped, conditions allowing for strict scientific control.

Cortisone is a convenient short word for the adrenal cortical hormone, 17-hydroxy-11-dehydrocorticosterone. It was first isolated by Dr. Kendall from the adrenal cortex in 1935, and he was largely responsible for its partial synthesis, the final stages being completed by Dr. Lewis H. Sarett in the Merck laboratories. At the New York Congress Dr. Hench said that in addition to

the remarkable effect in rheumatoid arthritis cortisone alleviated the arthritis associated with psoriasis and also that accompanying lupus erythematosus. Encouraging results had also been obtained in three cases of rheumatic fever. Professor Richard H. Freyberg, of Cornell University, reported good results in the treatment of Strumpell Marie spondylitis. According to Dr. Edward W. Boland, a patient who was bedridden, walked and fed herself within forty-four hours of starting treatment. 'After nine days of treatment she literally danced a jig.' Professor Walter Bauer, of the Harvard Medical School, from his own experience confirmed the findings of other observers. Another important point is that, because of the euphoria and increased mental capacity of those receiving cortisone, workers at the Mayo Clinic are investigating its effects on sufferers from mental disorder.

It must be stressed that in the treatment of rheumatic conditions cortisone is not a cure any more than insulin is for diabetes. Withdrawal of the hormone from a patient with rheumatoid arthritis leads to a relapse into crippledness. For those who want to treat this disease and for those who want to be treated it is therefore not just a question of injecting a few hundred milligrams of an extremely scarce drug in order to be cured; it is a question, so far as is known now, of being able to maintain treatment indefinitely.

Antibiotics in Primary Atypical Pneumonia

(Abstracted from the *Lancet*, ii, 16th July, 1949, p. 110)

PRIMARY atypical non-bacterial pneumonia, or virus pneumonia, has only been recognized as a clinical entity during the last fifteen years or so.

Until recently there was no specific treatment, the sulphonamides, penicillin and streptomycin all being ineffective, except possibly in preventing complications, although even for this the evidence is scanty. It is known that aureomycin and chloromycetin ('Chloramphenicol'), two new antibiotics introduced in 1948, are effective in some virus infections, such as psittacosis and lymphogranuloma venereum. Their antiviral action suggested their trial in primary atypical pneumonia. Several favourable reports have already appeared on the treatment of the disease with aureomycin.

At the moment the case for chloromycetin is not quite so strong. This antibiotic is effective by mouth, is practically non-toxic, and is now obtainable in this country as a result of its recent synthesis.

Clinical Intoxication with Potassium: Its Occurrence in Severe Renal Insufficiency

By M. M. KEITH

and

H. B. BURCHELL

(From the *American Journal of Medical Sciences*, January 1949, Vol. 217, p. 1, as abstracted in the *Journal of the American Medical Association*, Vol. 140, 11th June, 1949, p. 559)

KEITH AND BURCHELL report 13 cases of potassium toxæmia in 13 patients between the ages of 17 and 61 years with acute, subacute and chronic forms of bilateral diffuse nephritis. All patients died and the clinical diagnosis was confirmed at necropsy in 10 cases. Potassium salts were administered as diuretic agents to 3 of the patients, 2 of whom had œdema, and toxic effects resulted. Certain clinical symptoms such as paræsthesias of the hands and feet after the ingestion of the potassium salts suggested the possible presence

of potassium intoxication. The actual proof of the potassium intoxication rests on the demonstration of a co-existing hyperpotassemia and a characteristic electrocardiographic sequence in the following order of appearance: increased height of the T wave; a QRS of increased width; loss of P waves; gross intraventricular conduction defects, the electrocardiogram superficially simulating bundle branch block; cardiac arrest with irregular undulating potentials of low voltage. The serum potassium in the authors' cases varied from 7.7 to 10.5 milliequivalents per litre. Potassium toxemia produces a serious condition in the myocardium, which may be reversible but also can lead to fatal cardiac standstill. Beneficial therapeutic procedures such as the use of calcium and sodium salts and solutions of dextrose and blood can be applied and are particularly indicated in patients with early potassium intoxication. The administration of potassium salts to patients with severe renal insufficiency may be a dangerous procedure.

Poisoning from Aniline Marking on Diapers

(From the *Journal of the American Medical Association*, Vol. 140, 25th June, 1949, p. 684)

KAGAN and his co-workers have warned against the hazard of aniline intoxication in infants, particularly premature infants, from the use of diapers stamped with inks containing aniline dyes. Sixty-three such cases have been reported of which five terminated fatally. Kagan and his group have added 9 cases to this series. Aniline may be absorbed through the skin. In the body it produces cyanosis through conversion of hemoglobin to methemoglobin, a non-oxygen-carrying pigment. Such conversion is slow, and prolonged absorption of the dye is required to produce a significant effect. Infants, especially premature infants, are particularly susceptible to diminished supply of oxygen and hence even slight degrees of methemoglobinemia may be serious. Prevention of such accidents is simple. If the diapers are boiled after they are stamped and thoroughly dried before use, the dye becomes fixed and absorption does not occur. The ideal method of prevention would be the use of non-toxic dyes, but unfortunately, vegetable pigments, charcoal and silver nitrate lack the permanence required for marking clothing in large institutions.

Peroral Administration of Undecylenic Acid in Psoriasis

By H. H. PERLMAN
and
I. L. MILBERG

(Abstracted from the *Journal of the American Medical Association*, Vol. 140, 9th July, 1949, p. 865)

Forty-one psoriatic patients were treated with undecylenic acid perorally. Many of these patients were suffering from recalcitrant forms of the disease. No external medication was used.

The standard dose eventually adopted, which was also the highest daily dosage attained, was 19.8 gm. of the acid, in the form of 45 pearls of 0.44 cc. each, i.e. 3 times 15 pearls per day. The ingestion was found free from serious or lasting toxic effects. Mild gastrointestinal disturbances occurred, but only in one instance did these interfere with the continuation of the treatment schedule.

Of 40 psoriatic patients with cutaneous lesions, 12 showed unequivocal improvement during treatment, 15 were somewhat improved, 10 evidenced no change,

and 3 had distinct aggravation of the disease. Seven of 8 patients with psoriatic arthropathy noted relief from pain.

It appears possible that undecylenic acid had favourable influence on the course of some of the cases in the improved group observed. Much further investigation will be needed before definite conclusions can be drawn. The object of the report is to submit the method and its many possible modifications for more extensive clinical evaluation and further fundamental study.

Dangers of Intrathecal Medication

By G. WILSON *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 140, 30th July, 1949, p. 1076)

The occurrence of serious neurologic complications following intrathecal administration of many anesthetics, drugs, serums and antibiotics illustrates the grave potential dangers of intrathecal administration. The use of this portal is illogical for most therapeutic agents and may be unnecessary for all. Consideration must be given to whether the benefits obtained outweigh the risk of the grave complications which may ensue.

Synergistic Action of Penicillin and Streptomycin on *Endamoeba Histolytica* Cultures

By H. SENECA *et al.*

(From the *American Journal of Tropical Medicine*, Vol. 20, January 1949, p. 37, as abstracted in the *Journal of the American Medical Association*, Vol. 140, 30th July, 1949, p. 1120)

SENECA and his co-workers found that neither penicillin nor streptomycin is amebicidal in concentrations of 100 to 1,000 units per cubic centimetre. A combination of the two in equal unitage kills amebas in the first generation at a total concentration of 2,000 units per cubic centimetre, and in the second generation at 1,000 units per cubic centimetre. The latter concentration is found not to be bactericidal; hence the action is probably a direct one rather than an elimination of necessary bacterial products. The authors suggest that the combination of penicillin and streptomycin may have therapeutic usefulness, especially in preference to intrinsically more toxic agents, such as emetine hydrochloride. Such a therapy might be expected also to destroy the secondarily invading bacteria, with clinical benefit.

Chloroquine and Hepatic Amebiasis

(From the *Medical Journal of Australia*, Vol. II, 9th July, 1949, p. 63)

The antiplasmodial activity of chloroquine is well established and the drug has been used extensively in the suppression of malaria. It was known that chloroquine was highly concentrated in the liver, found to a much lesser degree in the intestinal walls and excreted in the faeces only in small amount. Because of these properties, N. J. Conan, junior, in setting out to determine whether the drug had antiamoebic activity, decided that amoebic infection of the liver rather than

of the colon would be the test object of choice. His results are striking. He presents a detailed account of eight patients with hepatic amœbiasis who were all successfully treated with chloroquine, seven by himself and one by F. Murgatroyd, of London. He quotes also the results of other investigators, communicated personally to him, which bring the total number of patients with hepatic amœbiasis cured by means of chloroquine up to 22. The evidence indicates that it is at least as effective as emetine and lacks the toxicity which is such a disadvantage of the latter drug. On the basis that it is theoretically highly desirable to treat every patient with intestinal amœbiasis with agents designed to eradicate amœbæ wherever they may be in the body, a practice not feasible when emetine was the only available agent for treating extra-intestinal amœbiasis, Conan recommends that chloroquine be employed in addition to a more efficient intestinal amœbicide for the treatment of all patients with intestinal amœbiasis. Conversely, for the treatment of hepatic amœbiasis, an intestinal amœbicide should always be employed in addition to chloroquine. Conan's results appear to confirm his confidence in such a combination not only for treatment, but also for purposes of diagnostic and therapeutic tests.

Isopropylpinephrine and Bronchial Asthma

(Abstracted from the *Medical Journal of Australia*, Vol. II, 30th July, 1949, p. 173)

AN isopropyl modification of adrenaline (or epinephrine, as it is normally called in the United States) has recently achieved some prominence. This drug, racemic 1-(3-4-dihydroxyphenyl)-2-isopropylaminoethanol, has been named variously 'I.P.A.', 'Aleudrin', 'Aludrine', 'Isorenin', 'Isonorin' and 'Isuprel'. The clinical evaluation of its use in the management of bronchial asthma has been the subject of a report by L. N. Gay and J. W. Long. They describe isopropylpinephrine as 'a sympathomimetic amine capable of bronchial-dilating action in bronchial asthma when administered by mouth, sublingual absorption, inhalation and subcutaneous injection'. Gay and Long have administered the drug in a variety of ways to a large series of patients of different types and ages and under varying conditions. They found a wide variation among patients in both therapeutic response and occurrence of side actions. The inhalation of a nebulized mist of aludrine of strength 1 : 200 proved to be the best method of administration, generally affording relief from asthma of all grades of severity with an incidence of side effects of only 4 per cent. Aludrine in this form greatly facilitated the liquefaction and excretion of sputum in the presence of chronic asthma. Sublingual absorption of 10-milligramme pellets is stated to be the second method of choice because of its convenience and speed of action and the fact that the patient can discard all undissolved drug in the event of serious side effects. The 'sublinguet' was of greatest value in the early abortion of mild asthma, of less benefit in moderate asthma and of no benefit in severe asthma; 33 per cent of users experienced mild and fleeting side actions. The routine use of aludrine by mouth was found to be impractical because of the high incidence of side effects (75 per cent) with use of the minimum effective dose (15 milligrammes). In general, Gay and Long state, the relief afforded does not justify the unpleasant symptoms associated with its oral administration. With regard to subcutaneous injection, the use of a concentration of aludrine of 1 : 1,000 is regarded as potentially dangerous, as shown by the high incidence of pronounced side effects and the demonstration of changes in electrocardiographic patterns; but for selected patients, doses of 0.3 to 0.5 millilitre of aludrine solution 1 : 5,000 are considered to be safe and practical, having a therapeutic efficacy about equivalent to the customary doses of adrenaline solution 1 : 1,000.

Experience has shown that aludrine by inhalation and injection is effective for those patients no longer responding to adrenaline. The subcutaneous injection of aludrine solution 1 : 1,000 causes pronounced tachycardia and increase in pulse pressure, with moderate rise in systolic and fall in diastolic blood pressure levels; in 1 : 5,000 concentration it causes a slight increase in cardiac rate and a slight elevation of systolic blood pressure, the diastolic pressure generally remaining constant. Overdosage by mouth or subcutaneous injection and therapeutic doses given by the same routes to sensitive persons may produce symptomatic and electrocardiographic evidence of coronary insufficiency; given sublingually or by inhalation in therapeutic doses, it produces no subjective evidence of coronary insufficiency. Altogether Gay and Long's report is comprehensive from the purely clinical viewpoint and warrants study by those who desire more detailed information. It provides practical guidance, the significant points of which we have indicated, in the use of a new and clinically useful drug.

Paracholera

(From the *Medical Officer*, Vol. 81, 4th June, 1949, p. 232)

THE *Chronicle of the World Health Organization* of March 1949, contains two short notes on paracholera (El Tor) which, though of little immediate interest to European epidemiologists, is indirectly of profound significance. Cholera is due to the vibrio which Koch discovered over 60 years ago. It was soon shown that this specific vibrio was one of a large genus of wide distribution, many species of which were common in waters and were harmless to man. The vibrio of Koch had become fixed and it alone could produce cholera. This was the position as it appeared to be 30 years ago, and was comparable to that of all other specific parasitic diseases. But research has shown that the matter is not so simple, and as our knowledge grew, it got more and more complex. Before we had bacteriology, physicians had separated from the diarrhoeas a particular form which they called typhoid. The bacteriologist showed that this was due to a specific parasite not concerned with other diarrhoeal reactions. It was then shown that there were other forms of typhoid, clinically indistinguishable, due to allied, but not identical, parasites. These came to be known as paratyphoids. It was then discovered that there were still other typhoid-like diseases, less like true typhoid clinically, due to other parasites less like the true typhoid parasite, belonging to species which commonly cause poisonings and it seemed that some of these species were apparently altering in the reactions they produce in their hosts. Thus *Salmonella typhimurium*, which gave a 'typhoid' in mice, attacked man, in whom it produced a poisoning but not a typhoid. But recently it has, with increasing frequency, given in man a 'disease', different from a 'poisoning', which is becoming more like a true typhoid. Later it was shown that the parasite of true typhoid (*Eberthella typhosa*) occurred in a numerous varieties which though they all produced similar clinical reactions in man were antigenically distinct. Much the same holds for most parasitic diseases.

We are now aware that continuous and somewhat rapid changes occur in the clinical manifestations of reactions to parasites, and the parasites also change, in their turn also producing different clinical manifestations. The description of typhoid given by the textbooks of forty years ago do not serve to-day in all particulars. At the end of this century it might be impossible to identify the typhoid of 1909 with that of 1899 and the parasites causing it may also be dissimilar. Cholera to-day is much the same as it was in Koch's day and is due to the vibrio he described. But in the Celebes and elsewhere a form of disease has

been discovered much like, but not identical with, true cholera due to a vibrio much alike, but not identical with that of true cholera.

New varieties of disease are described weekly. The general view is that the detection is new, but the phenomena are old; but the validity of this view is challenged, because as the new varieties appear the old varieties disappear. All this appears very awkward, but it is no good getting peevish about it. We must recognize that the phenomena of disease are subject to continuous evolution and what serves us to-day may be useless a short time hence.

Oral Administration of Aureomycin in the Treatment of Gonorrhœa

By C. H. CHEN *et al.*

(Abstracted from the *Urologic and Cutaneous Review*, Vol. 53, July 1949, p. 394)

A 100 PER CENT success was obtained in treating twenty unselected gonorrhœa patients with 6 grammes of aureomycin given orally in divided doses in 2 days, whereas the percentage of success was 90 in another series of twenty unselected gonorrhœa patients treated with a single injection of 300,000 units of penicillin in oil and wax.

An additional case of gonorrhœa who failed to respond to 20 intramuscular injections of 300,000 units of penicillin G in oil and wax and who recovered rapidly with oral aureomycin treatment is presented in detail.

Attention is called to the reported effectiveness of aureomycin in all five venereal diseases and its potential usefulness as a general oral prophylactic for these infections.

The Present Status of the Treatment of Thyrotoxicosis

By W. H. BEIRWALTES

and

C. C. STURGIS

(Abstracted from the *Practitioner*, Vol. 162, June 1949, p. 486)

THE administration of iodine followed by subtotal thyroidectomy may be employed in patients with uncomplicated exophthalmic goitre who have only mild toxicity. A far more satisfactory result is attained, however, by the use of propylthiouracil plus iodine. This group also has the highest incidence of 'cure' with propylthiouracil and iodine alone.

The optimum pre-operative treatment of patients with both nodular and non-nodular goitres of moderate to severe toxicity is 300 mg. of propylthiouracil and 4 drops of Lugol's solution per day. This should be continued until the basal metabolic rate is at least zero.

All large exophthalmic goitres and all nodular toxic goitres should be removed surgically.

Propylthiouracil with iodine may be used alone in an attempt to produce a 'cure' in the remaining patients, and in cases with high surgical mortality, with an 80 per cent chance of success in a selected group.

The indications for radio-active iodine are those for propylthiouracil with other limitations, such as possible danger to the patient and the difficulties of securing the material and controlling its use. Further experience with this form of therapy, under carefully

controlled conditions, is necessary before it can be recommended for widespread use. The chief use of iodine to-day in treating patients with thyrotoxicosis is in augmenting the anti-thyroid effect of propylthiouracil and in reducing the hyperplastic changes produced with propylthiouracil pre-operatively.

The Bacteriology of Food Poisoning

By G. S. WILSON

(Abstracted from the *Practitioner*, Vol. 162, June 1949, p. 445)

TOWARDS the end of last century, Brieger put forward the suggestion that food poisoning was due to the presence in the food of toxic amines or *ptomaines* formed as the result of bacterial putrefaction. This explanation had to be abandoned when it was found, firstly, that most food shown to be responsible for poisoning was perfectly normal in appearance and flavour, and secondly, that putrefied food could often be eaten with impunity. Further observations revealed in many outbreaks of food poisoning an organism belonging to the group now known as *Salmonella*—so-called after the American worker Salmon, who described the first member—and for many years it was held that food poisoning was essentially a salmonella infection.

When it became apparent, however, that numerous outbreaks were occurring from which organisms of this group could not be isolated, bacteriologist began to turn their attention to other possible causes. It was then that the enterotoxin of the common nose and skin organism, *Staphylococcus aureus*, was re-discovered and its significance appreciated. This finding was of double interest. It showed not only that food poisoning might be caused by an organism other than *Salmonella*, but that the mode of origin of the two types of poisoning was different. *Salmonella* multiply in the intestinal tract and give rise to a true infection, becoming manifest in twelve to twenty-four hours. *Staphylococci*, on the other hand, multiply in the food before it is eaten, producing an irritant toxin which gives rise to symptoms within two to four hours. The first type is now referred to as the 'infection' type, the second as the 'toxin' type of food poisoning.

More recent studies have rendered it probable that there is a third type falling somewhere between the other two. Thus in some outbreaks from which no salmonellæ or staphylococci can be cultivated, enormous numbers of an organism usually regarded as non-pathogenic, such as *Streptococcus viridans*, *Proteus vulgaris*, or a member of the paracolon, aerobic spore-bearing, or anaerobic spore-bearing groups, have been demonstrated. The inference is that these organisms, which are quite harmless when ingested in small numbers, are able to cause gastro-intestinal irritation when they have been allowed to proliferate abundantly in certain types of food.

Salmonella food poisoning.—The illness is characterized by headache, nausea, vomiting, abdominal pain, and diarrhœa. Fever is usually present, and lasts for two to five days. Nausea and vomiting are not as a rule prominent symptoms, as they are in the staphylococcal type of food poisoning, and they may be absent. The patient is generally better within a week, but a fortnight often elapses before he is really strong again. Occasionally the organisms invade the blood stream and give rise to a fatal infection of the heart or meninges.

Sources.—*Salmonella* are pathogenic for a wide variety of domestic animals and birds, and that these constitute the main reservoir of infection for man. Rats and mice also suffer from infection with salmonellæ, and numerous outbreaks in human beings are on record that have been traced to contamination of food from rodent droppings.

Although animals constitute the primary source of infection, a great deal of food poisoning is spread by human agency. Ambulant cases and transitory carriers of salmonellæ appear to be not uncommon, and when employed in the preparation or distribution of food, they may transmit infections to other persons.

Practically any food can act as a vehicle for the transmission of salmonella infection, but the most common articles are those which are prepared in such a way as to enable any organisms that have gained access to them to multiply. Thus made-up meat and fish preparations, such as pressed beef, brawn, sausages, pies, and rissoles, are often implicated. Ducks' eggs are particularly dangerous, and spray-dried egg, unless eaten soon after reconstitution and thoroughly cooked, is also liable to cause infection. Truffles, ice cream, synthetic cream and milk figure not infrequently, but freshly cooked meat, bread, vegetables, and fruits seldom act as vehicles of infection. Canned meat is usually sterile but may of course become contaminated after removal from the tin.

Staphylococcal food poisoning.—The clinical picture of staphylococcal food poisoning is often so distinctive as to leave little doubt of the diagnosis, even in the absence of bacteriological investigation. Since the toxin is preformed in the food, symptoms come on soon after ingestion. The usual incubation period is two to four hours. The attack begins with dizziness, headache, nausea and vomiting. Abdominal pain may or may not be present, and vomiting is more conspicuous than diarrhoea. The temperature is generally normal or, in the later stages, subnormal. In severe cases the patient vomits continually, is unable to retain his equilibrium, and passes into a state of collapse, in which he lies motionless, with a cold, clammy skin, shallow respirations, and the appearance of impending death. Cases seldom prove fatal, however, and recovery is surprisingly rapid. Many patients are quite well again within twenty-four hours.

Sources.—Food becomes contaminated with staphylococci from human carriers.

The mere contamination of the food with an enterotoxin-producing strain of *Staph. aureus* is not sufficient to render the food poisonous. The organisms must multiply abundantly before sufficient toxin is formed to cause symptoms.

The most favourable vehicles are much the same as those implicated in salmonella infections, namely made-up meat dishes, truffles, layer cakes, custards, and ice cream. In every instance the food is found to have been left for some hours at a temperature favouring bacterial multiplication.

Food poisoning due to other bacteria.—Some outbreaks of food poisoning occur in which the most careful examination of the food and of the patient's excreta fails to reveal the presence of either salmonellæ or staphylococci. The causation of these outbreaks is still in doubt. Clinically, the symptoms tend to be mild and to come on about eight to sixteen hours after the suspected meals. Nausea and vomiting are usually inconspicuous, and neither the abdominal pain nor the diarrhoea is severe. Recovery is generally complete within a day or two.

Tick-borne Relapsing Fever in Kashmir

By K. N. A. RAO

and

S. L. KALRA

(From the *Current Science*, Vol. 18, July 1949, p. 249)

The existence of relapsing fever in Kashmir was first detected early in 1948. Previously the disease had remained unrecognized due to its mild symptoms, no fatality, and resemblance with malaria. Two species of

Ornithodoros ticks, *O. crossi* and *O. lahorensis*, were found widespread in the State, particularly infesting the animal quarters. *O. crossi* were found infected in nature and the disease conveyed to guinea-pigs by their bite was similar to that produced by human strains from local cases. It attacked man far more readily than *O. lahorensis*, also the bite marks on patients resembled those of the former. On the other hand, naturally infected specimens of *O. lahorensis* have not been found here so far, and lice could not be infected with the local strains. Therefore, it was considered that the vector of relapsing fever in Kashmir was *O. crossi*. Detailed investigations will be published elsewhere.

The Effect of Chloroquine Diphosphate on Malaria Splenomegaly

By D. A. BERBERIAN

and

E. W. DENNIS

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 29, July 1949, p. 463)

WEEKLY administration of suppressive doses (0.5 gm.) of chloroquine diphosphate, without recourse to antimosquito measures, not only effectively controlled malaria in the village of Saideh, Lebanon, but reduced the splenic index from 59 to 6, and the average size of enlarged spleens (AES) from 1.9 to 0.12, within an average treatment period of 26 weeks.

The splenic index decreased only from 70 to 50 during the corresponding period of eight months when effective malaria control was established for the neighbouring village of Amik by means of D.D.T. residual spray.

Chloroquine diphosphate can be administered in weekly suppressive doses for at least seven months without undesirable side-effects, even in pregnancy, and is recommended for the treatment of splenomegaly due to chronic malaria.

It is concluded that malaria eradication within a single season will be facilitated by the combined operation of mass suppressive medication with chloroquine diphosphate and appropriate application of D.D.T., thereby simultaneously reducing both the human and insect reservoirs of the disease.

Methods of Pinworm Diagnosis

By P. C. BEAVER

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 29, July 1949, p. 577)

THREE types of anal swabs for the diagnosis of *Enterobius vermicularis* infection were studied: (i) The NIH cellophane swab as described by Hall, (ii) the wet pestle swab as described by Schöffner and Swellengrebel, and (iii) the transparent adhesive cellulose tape as suggested by Graham, but used in the manner first described by Jacobs, and prepared for microscopic examination in a manner described as new in this paper, the essential feature of the new modification being the use of toluene to clear the preparation.

On a small series of transparent adhesive tape specimens it was found that using a drop of toluene between the slide and the tape to clear the preparation increased the positive findings by an average of 21 per cent and decreased the time necessary for examination by an average of 40 per cent.

Of 236 positive specimens obtained by simultaneous use of the NIH and wet pestle swabs, 91.5 per cent were diagnosed by wet pestle as compared with 75 per cent by NIH swab. Respectively, the pestle and NIH preparations averaged 88 and 52 eggs per preparation.

Of 160 positive specimens obtained by simultaneous use of the wet pestle and transparent tape, 76.3 per cent were diagnosed by wet pestle and 95.6 per cent by transparent tape. Respectively, the pestle and tape preparations averaged approximately 50 and 1,000 eggs.

The greater efficiency of the tape technique was found to be due in part to the ease with which the novice can be taught to use it properly. Some of the physicians, nurses, medical students, parents and matrons made frequent serious technical errors in the use of the others but all were about equally efficient in taking specimens with the transparent adhesive tape.

'P-A-S'

(Para-amino-salicylic Acid)

(From the *Medical Review*, Vol. 43, July 1949, p. 106)

THIS is a chemotherapeutic agent which inhibits the growth of tubercle bacilli. It is used for the treatment of certain forms of tuberculosis.

At the Annual Conference of the British Tuberculosis Association, 1948, it was reported that in a large series of cases of tuberculosis, many of them with advanced disease, improvement was noted in more than 50 per cent. The most striking effect was an improvement in general well-being coinciding with an increase in weight, raised haemoglobin, and a fall in the blood sedimentation rate. Improvement in the radiological appearances was seen in the exudative type of disease, but in the more chronic cases cavities were little effected. The treatment, however, made it possible for many of these cases to have coincident or subsequent collapse therapy. Toxic effects were not usual, though some patients exhibited vomiting and diarrhoea. The drug was given orally in doses of 14 gm. daily (for an adult) divided into four or six doses. It was rapidly absorbed and excreted and a blood concentration of 3 to 6 mg. per millilitre should be maintained. Treatment could be continued for several months, and bacterial resistance to the drug did not occur. The blood sedimentation rate was the most sensitive indicator of the management of treatment. (Ward, Blenkinsop and Co., Ltd., 6, Henrietta Place, London, W.1.)

Plague

By DR. GEORGES BLANC

Director of the Pasteur Institute of Morocco

(Reproduced from W.H.O. Special Features, No. 4, issued by Public Information Office, Pan-American Sanitary Bureau Regional Office, World Health Organization, 2001 Connecticut Avenue, N.W., Washington 8, D.C.)

THE history of plague is a long and dark one. Even to-day the name itself, with its association of swift and widespread death, brings terror to the people of many lands. So sudden were its visitations in Europe that Ambroise Paré, a famous French physician of the sixteenth century, called the malady 'tempestuous'.

Coming out of Asia, plague first invaded Europe, via Byzantium, in the sixth century, during the reign of the Emperor Justinian. It was then that Procopius, the Byzantine historian, gave a precise description of

the effect of plague on the human body, observing that it brought about blood-poisoning and inflammation of the lymphatic glands.

After several successive waves of plague had spread over Europe, the disease appeared to lie low for nearly three hundred years. Then, in the fourteenth century, the terror revived. This was the time of the 'Black Death' which devastated Europe, wiping out over a third of the total population. Time and again the terror struck, the attacks continuing until the eighteenth century. When in 1720 it re-entered Marseilles to claim 40,000 victims, it had already left hundreds of thousands dead in its path, including 70,000 in the London of 1665.

CRUDE DEFENCE IN MIDDLE AGES

The panic created by the mysterious disease led to the adoption of crude methods of defence. Infected houses were fumigated and marked with a cross, and no one was allowed to enter. Doctors wore cowls, and their clothes also bore the sign of the cross. People stepped back at their approach with apprehension, or even with hostility.

It was forbidden for anyone from an infected zone to enter a healthy city. Those caught attempting to do so were turned back after having their ears cropped. The sight of persons whose ears had been cut off was not uncommon.

The rapid and unpredictable movement of the 'Black Death' gave rise to rumours that it was being deliberately spread. The accusation was made that fat from corpses was being smeared on the doors of houses. Many unfortunates were declared to be guilty of this offence and put to death.

Plague was believed to be a manifestation of divine wrath and the saints were called on to intercede on behalf of mankind, the most celebrated being St. Roch, popular pictures of whom are still to be seen showing him with the thigh gland enlarged—a symptom of the disease—and at his feet the dog that had saved him from starvation when he was cast out as plague-stricken.

The many parishes of St. Roch to-day bear witness to the fact that plague had visited them, and so caused them to adopt the saint's name in the hope of obtaining his personal intercession.

The realization that plague was spread through contagion developed with increasing force, and in the fifteenth century the Venetians set up the first isolation ward and created quarantine.

ERADICATION FORESEEN TO-DAY

Although plague left Europe in the eighteenth century, it has remained in the Orient where its ravages still continue. 100,000 died of it in Canton in 1894. In the same year it reached Hong Kong, where Yersin showed that the bacillus was identical with that found in infected rats. Finally, in 1898, Simond demonstrated that the disease is carried by the rat flea.

Within a few further years all the relevant facts about the disease were co-ordinated, and shortly after was added knowledge of the type of infection carried by wild rodents, now known as sylvatic plague. By now the fight against the 'Black Death' had commenced along planned lines by means of destruction of rats, isolation of individuals in contact with infected persons, quarantine, and the use of treatment sera and preventive vaccines.

In recent years great progress has been made. The discovery of powerful insecticides such as DDT, and of efficient therapeutics such as the sulpha drugs and streptomycin have given greater hope for conquering this age-old scourge. The World Health Organization has formed an Expert Committee on Plague for the purpose of combining all known methods of attack against what was once an almost unknown enemy. During the recent meeting of this Committee, held

at W.H.O. Headquarters in Geneva, a system was planned for the compilation and assessment of all existing data, the carrying out of full treatment measures and the detailing of methods of eradication of plague centres.

It is planned that a group of specialists in this field will be sent to India, where the disease to-day presents a very grave problem. There they will demonstrate plague eradication work for the first time on an international scale. Other demonstration areas for plague eradication recommended by the W.H.O. Expert Committee include one of the infected islands off the coast of Africa (Azores or Madagascar), Morocco, the Belgian Congo, and China.

In these plague centres the use of DDT, '1080' (sodium fluoracetate), and streptomycin, combined with the expert knowledge available to-day, will demonstrate in actual practice the ability of modern science to conquer one of man's most dreaded enemies.

Temporary Relief of Asthma by Jaundice

By N. GORIN

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 24)

In any chronic disease characterized by exacerbations and remissions and in which so many variable factors may play a part, some of which may be psychic, any claim to clinical relief must be accepted with considerable caution. The author has presented three cases of intractable asthma in each of which the development of jaundice was associated with decided remission of symptoms. One can only speculate as to the cause of this and note the remarkable analogy between the relief obtained in cases of rheumatoid arthritis and that seen in chronic asthma. Also, in these two groups of devastating sickness, there lie within the person certain reparative powers, the nature of which are as yet unknown, apparently released by alterations in hepatic function. The 'reversibility' of disease processes that are frequently regarded as almost hopeless is of interest. The similarity of the relief obtained in these two groups of diseases immediately raises many questions as to their common denominator and as to the underlying mechanism for this dramatic change. Certainly, the observation calls for animal experimentation and further clinical study, both of which have already been started.

Reviews

THE CLINICAL APPRENTICE: A GUIDE FOR STUDENTS OF MEDICINE.—By John M. Naish, M.D. (Cantab.), M.R.C.P., and John Apley, M.D. (Lond.), M.R.C.P. 1948. John Wright and Sons Limited, Bristol. Pp. x plus 200. Illustrated. Price, 15s.

This book is meant for students receiving their clinical training in medicine. The authors have tried to keep readers of this book by the bedside, where the craft of medicine can truly be mastered. There are two sections, section 1—examination at leisure and section 2—examination of acute cases. After a general survey, the various systems of the body are considered from the point of view of the clinical approach and a helpful concluding section considers the problem of acute cases. Coma, meningismus, hyperpyrexia, dyspnoea and fits are briefly discussed. The book will prove a useful introduction to beginners.

R. N. C.

CARDIOVASCULAR DISEASE IN GENERAL PRACTICE.—By Terence East, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Third Edition. 1949. H. K. Lewis and Company, Limited, London. Pp. x plus 208, with 34 illustrations. Price, 15s.

THE fact that a third edition of this valuable little book has been needed in little over three years is ample proof of its popularity. Throughout, the physiological approach to the problem is maintained. In this new edition some additions have been made and the whole has been brought up to date. In dealing with treatment of thyrotoxic heart, the author states that septic tonsils should always be removed before thyroidectomy.

This is a book which can be recommended to the practitioner and post-graduate student.

R. N. C.

TUBERCULOSIS INDEX AND ABSTRACTS OF CURRENT LITERATURE. QUARTERLY, JUNE 1949, VOL. 4, NO. 2.—By National Association for the Prevention of Tuberculosis, Tavistock House North, London, W.C.1, England. Price One Guinea or Five Dollars per year

THE Tuberculosis Index appears quarterly. It is primarily a list containing important articles in the scientific, medical and social literature of this subject. The more significant articles are abstracted by specialists. The table of contents has been revised and rearranged in this issue, and covers the vast field in over thirty-one sections. The tuberculosis workers will find it very useful.

R. N. C.

SYNOPSIS OF PÆDIATRICS.—By John Zahorsky, A.B., M.D., F.A.C.P. Assisted by T. S. Zahorsky, B.S., M.D. Fifth Edition. 1948. The C. V. Mosby Company, St. Louis. Pp. 449, with 158 text-illustrations and 9 colour plates

THOUGH a synopsis, this book is written in a readable form, giving a mass of practical information of diseases of children. In the first few chapters the growth, hygiene of infancy, nutrition and feeding are described. Then follow two useful chapters on diagnosis and therapeutics, and after this comes the main part of the book which is concerned with diseases and their management. In this edition the book has been enlarged, and a few new sections have been added to some chapters. There are many good illustrations. It reflects the modern practice in paediatrics, is of convenient size and can be recommended to students and practitioners of medicine.

R. N. C.

A TEXTBOOK OF MIDWIFERY.—By Wilfred Shaw, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G. Third Edition. 1949. J. and A. Churchill Limited, London. Pp. xiv plus 649. Illustrated. Price, 22s. 6d.

THIS book continues to be what it was when we had the pleasure of reviewing the previous edition. The great merit of this book lies in its practical teaching. Controversial points and academic discussions of an entirely theoretical nature have been carefully excluded. This is of great value to the student preparing for an examination. A busy practitioner gets immense satisfaction when he has to refer to this book to revise his memory; he is spared the trouble of going through various theoretical preambles before reaching his special point of enquiry.

The printing and the get-up are similar to those of the former edition.

M. N. S.

A HISTORY OF THE HEART AND THE CIRCULATION.—By Fredrick A. Willus, M.D., M.S. (In Med.), and Thomas J. Dry, M.A., M.B., Ch.B., M.S. (In Med.). 1948. W. B. Saunders Company, Philadelphia and London. Pp. xvii plus 456. Illustrated. Price, 40s.

This is an account of the historical development of our knowledge of the heart and circulation from the ancient to the modern times. The story begins some 5,000 years back, when the practice of mummification gave the Egyptians opportunities to observe the structures within the body cavities. They possessed a general idea of the heart and blood vessels. They also recognized and counted the pulse, and employed it in evaluating the status of the heart. There were subsequent contributions from other countries as well, but the observation and deductions of the ancient were very superficial and often fallacious. Nevertheless, they paved the way and stimulated the interests of the scientists who were destined to follow. The authors review the successive eras and introduce us to the illustrious personalities whose contributions were important in the gradual clarification of the mysteries of the heart and circulation, and their diseases. We learn also of the development of cardiac therapy and surgery, and of the discoveries of modern methods of diagnosis such as auscultation by stethoscope, x-ray and electrocardiography. In reading through the book, one feels how our present unique position has been arrived at by contributions of teachers and clinicians over many centuries.

The second part of the book gives special and more detailed biographical accounts of a selected group of contributors from Hippocrates to Sir Thomas Lewis. The third part is devoted to a summary presentation of subject matter; this permits ready reference to the various subjects. The book is profusely illustrated, and provided with valuable references. It is of absorbing interest and should be read not only by cardiologists but by all practitioners of medicine.

R. N. C.

WARD ADMINISTRATION AND CLINICAL TEACHING.—By Florence Meda Gipo, M.S., R.N., and Gladys Seflow, Ph.D., R.N. 1949. The C. V. Mosby Company, St. Louis. Pp. 357. Illustrated.

This book is about nursing organization and teaching in hospital wards. The first part deals with administrative matters for the effective management of a ward, so far as the nursing service is concerned. The second part is concerned with the methods and procedures of clinical teaching. The two subjects have been combined because the two activities are too closely united in practice. Although meant for the U.S.A. nursing personnel, the book will interest our hospital administrators also who wish to know how these things are arranged in a country known for efficiency.

R. N. C.

THE NATIONAL HEALTH SERVICE.—By Charles Hill, M.D., and Jock Woodcock. 1949. Christopher Johnson Publishers Ltd., London. Pp. x plus 283 plus CL. Price, 16s.

On 5th July, 1948, Great Britain established under the National Health Service Act a comprehensive health service, making it available to every citizen. The British Medical Association opposed it but afterwards gave way, pending the settlement of several important questions. A scheme like this is bound to present many complications, one of which is that it is costing very much more than was originally estimated. The Act itself is a complicated one, and so are two regulations and directions issued under it. In this book Dr. Charles Hill and Mr. Jock Woodcock who have seen the creation of the service from the inside seek to explain as simply as possible to doctors and others concerned how the scheme works. The Act has been the subject of much controversy. By keeping away from the dispute, the authors give an unbiased inter-

pretation of the Act and the regulations made under it. The book will not have any special appeal for medical practitioners and administrators in this country, but those interested in socialistic medicine will get a lot of information from it.

R. N. C.

OPERATIONS OF GENERAL SURGERY.—By Thomas G. Orr, M.D. Now (Second) Edition. 1949. W. B. Saunders Company, Philadelphia and London. Pp. x plus 890 with 1,700 stop-by-stop illustrations on 721 figures. Price, 67s. 6d.

A very useful reference book for the general surgeon. The copious easily understood illustrations are valuable. Almost any problem facing a general surgeon has been discussed lucidly and helpfully. It is sure to be popular and instructive to every young general surgeon.

L. M. B.

AN ATLAS OF AMPUTATIONS.—By Donald B. Slocum, M.D., M.S. 1949. The C. V. Mosby Company, St. Louis. Pp. 562 with 564 illustrations.

How far artificial appliances can and amputated limbs to regain functions and so add to the comfort and usefulness of individuals who have been maimed, can be realized by going through this book and studying carefully every portion in order to appreciate the skill and knowledge required to make an artist scientific as differing from the 'butcher surgery'. This atlas is recommended to all orthopaedic surgeons.

L. M. B.

BASIC SURGERY.—By Amla Kumar Sen, M.D. (Cal.), D.P.H. (Lond.), F.R.C.S. (Eng.). First Edition. A. Mukherjee and Co., Ltd., Calcutta. Pp. xiv plus 542 with 198 illustrations. Price, Rs. 25 only.

A book with a novel title intended for undergraduate students. It contains almost everything that is necessary for the undergraduate to know and all unnecessary details are left out. The illustrations are also novel—in as much as they differ in a remarkable manner from those which have been in vogue with most books. The undergraduate will find in this book a useful volume when preparing for examinations.

L. M. B.

A TEXTBOOK OF SURGERY.—By American Authors. Edited by Frederick Christopher, B.S., M.D., F.A.C.S. Now (Fifth) Edition. 1949. W. B. Saunders Company, Philadelphia and London. Pp. xxv plus 1550 with 1,465 illustrations on 742 figures. Price, 65s.

A textbook with over 1500 pages is a formidable volume to undergraduates but the amount of information contained therein is so vast and discussions so nearly complete that if one attempts to reduce the size of the volume he will find the object of the book totally changed. The experiences of the leading American surgeons are embodied in a very masterly manner and wherever you turn you find authoritative information with all the recent advances in thought and practice.

L. M. B.

DOCUMENTA OPHTHALMOLOGICA—ADVANCES IN OPHTHALMOLOGY.—Edited by F. P. Fischer, A. J. Schaeffer and Arnold Sorsby. Vol. III. 1949. Uitgeverij Dr. W. Junk. S-Gravenhage. Pp. 328. Illustrated.

This volume comprises most of the papers read at the Conference on Colour Vision held at Cambridge in 1947. H. Hartridge writes on 'The polychromatic theory', W. D. Wright on 'The present status of the trichromatic theory', S. Polyak on 'Retinal structure and colour vision', W. E. Le Gros Clark on 'The laminar pattern of the lateral geniculate nucleus considered in relation to colour vision', R. Granit on

'The analysis of retinal elements by the micro-electrode technique', G. Wald on 'The photochemistry of vision', W. S. Stiles on 'Increment thresholds and the mechanisms of colour vision'. Further papers are E. N. Willmer on 'Colour vision in the central fovea', D. L. Macadam on 'Colour discrimination and the influence of colour contrast on acuity', J. G. Holmes on 'Colour recognition of very small light sources', D. B. Judd on 'Current views on colour blindness', The late S. Hecht on 'Brightness, visual acuity and colour blindness', F. H. G. Pitt on 'Some aspects of anomalous vision', S. Krauss on 'Phenomena observed in veiled colours', A. Ivanoff on 'Chromatic aberration of the eye', M. A. Bouman and H. A. Van Der Velden on 'The two-quanta explanation of the dependence of the threshold values on the visual angle and the time observation'.

The volume is thus an authoritative statement of the present position of the physiology of colour vision.

E. J. S.

THE PRACTICE OF REFRACTION.—By Sir Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Ph.D., M.D., F.R.C.S., Hon. D.Sc. (North Western). 1948. J. and A. Churchill Ltd., London. Pp. xiv plus 317 with 216 illustrations. Price, 18s.

THE fifth edition brings this excellent book up to date. New matter has been added on the nature and incidence of refractive errors and the recent views on their biological determination. This should help spread a more reasonable and national view of myopia. New knowledge of the transient changes in refraction has been added and aniseikonia is treated more fully. The sections on the mechanism of accommodation and anomalies of convergence have been revised. Descriptions of streak retinoscopy and velonoskiacopy have been added. This is one of the very best books on the subject and is written in elegant and very readable English. It is invaluable to the D.O.M.S. student.

E J S

OPHTHALMIC MEDICINE.—By J. H. Doggart, M.A., M.D. (Cantab.), F.R.C.S. (Eng.). 1949. J. and A. Churchill Ltd., London. Pp. vii plus 329 with 28 coloured plates and 87 text-illustrations. Price, 32s.

MANY ophthalmologists have been wondering when they would be able to purchase a new edition of Mr. R. Foster Moore's 'Medical Ophthalmology', the last edition of which was published in 1925. When Mr. Doggart was asked either to revise the 1925 edition or to write a new book, he chose the second alternative because there have been so many alterations in outlook during the last quarter century. So we say farewell to an old friend and a book of much individuality and distinction. We are however somewhat compensated by the new publication 'Ophthalmic Medicine'. It has not the same personality of the older book but it is much fuller and more subjects are dealt with. The illustrations are excellent and the text clear. It will become the standard book for ophthalmologists and one which will be read also with interest by physicians.

E. J. S.

CLINICAL PERIMETRY.—By H. M. Traquair, M.D., F.R.C.S. (Edin.). Sixth Edition. 1949. Henry Kimpton, London. Pp. xv plus 332 with 257 illustrations and 5 coloured plates. Price, 42s.

THIS book has been the standard work on the subject since the first edition was published in 1927 and it remains so. That the sixth edition has been printed only three years after the fifth, attests to its popularity. Two more coloured plates and two new illustrations have been added and the text revised and amplified. It is a masterly book and indispensable to all ophthalmologists. The printing, paper, illustrations and general layout are in every way up to Henry Kimpton's usual excellent standard.

E. J. S.

BOOK NOTICE

Souvenir of the 22nd Annual Conference, 1950, of the Madura Medical Association (Branch of the Indian Medical Association). Published by the Hon. Secretary of the Association. Pp. 159. Price, Rs. 2.

BESIDES containing the usual annual report, list of members, balance sheet, etc., this souvenir contains a list of medical officers in the district and eight contributions on medical and surgical subjects, e.g. recent advances in surgery, thoracic surgery, ectopic pregnancy, anaesthesia and low voltage contact x-ray therapy of early accessible cancer. There is also an interesting account of the experiences of a medical man as a Japanese prisoner of war. These contributions are the summaries of the lectures given at the monthly meetings of the Association.

BOOKS RECEIVED

1. The Deaf in India: Official Organ of the Convention of the Teachers of the Deaf in India. Editor A. C. Sen and Associate Editor B. K. Chakravarti. February 1950. Published by Sailendra Nath Banerjee from 50, Bondel Road, Ballygunj, Calcutta.

2. 5th All-India Dental Conference, Madras, 1950—Souvenir.

3. Ildigesto Medico: Selezione Di Medicina Moderna. Vol. 1, No. 2, December 1949. Dott. Pietro Chiara. Editor Piazza Matteotti, 7 Catania.

4. Chikitsa-Jagat. Vol. XXI, No. 4, February 1950. Editor Dr. A. D. Mukherji. Publishing Office: 27C, Upper Circular Road, Calcutta 9. Annual Subscription Rs. 4 and price per copy As. 8 only.

5. Health Service Areas—Estimates of Future Physician Requirements. Public Health Bulletin No. 305. Federal Security Agency Public Health Service, Washington, D.C.

6. Endeavour. Vol. IX, No. 33, January 1950. Editor E. J. Holmyard, M.A., M.Sc., D.Litt., F.R.I.C. Published by Imperial Chemical Industries Ltd, London, S.W.1.

7. Business Week India. Vol. 11, No. 44, 22nd October, 1949. Edited, Printed and Published by K. V. Panchanadam at the Business Week Press, 173, Lloyd Road, Madras 14.

8. British Journal of Urology. Vol. XXI, No. 4, December 1949. Editor David Band, F.R.C.S. (Edin.). Published by E. and S. Livingstone Ltd., 16 and 17, Teviot Place, Edinburgh.

9. The Indian Pharmacist. Vol. V, No. 4, January 1950. Editor Principal M. L. Schroff, A.B. Hons. (Cornel). M.S. (M.I.T.). Published by Prabha Schroff for Pindars Limited from 7, Lower Rawdon Street, Calcutta.

10. Report of the Botanical Survey of India for 1941-42. Printed by the Government of India Press, Calcutta, India, 1947.

11. Report of the Botanical Survey of India for 1942-43. Printed by the Government of India Press, Calcutta, India, 1948.

12. Report of the Botanical Survey of India for 1943-44. Printed by the Government of India Press, Calcutta, India, 1948.

13. Report of the Botanical Survey of India for 1944-45. Printed by the Government of India Press, Calcutta, India, 1948.

14. Report of the Botanical Survey of India for 1945-46. Printed by the Government of India Press, Calcutta, India, 1948.

15. Colonial Office: A note on some of the Scientific Studies undertaken by members of the

Colonial Medical Service during the period 1930-47, with a Bibliography. His Majesty's Stationery Office, London, 1949. One shilling net.

16. Indian Research Fund Association. Report of the nineteenth meeting of the Nutrition Advisory Committee of the Indian Research Fund Association held in the Central Secretariat, North Block, New Delhi, on the 22nd and 23rd November, 1949.

Correspondence

SUDDEN DEATH OF BABIES

SIR,—To the causes of 'Sudden Death of Babies' published in your November issue, I can add another cause from my personal knowledge. In this case, the mother was suckling her child of about 7 months on its side, the back being supported by a pillow to prevent its attaining the supine position and fell asleep. When the mother awoke she felt some pressure on her breast and when she tried to move the head of the child, she found it was dead. I saw the child after its death and was told that it was quite healthy before and the breasts of the mother were unduly long, soft and pendulous. Though not quite definite, I formed the opinion that the death was due to 'asphyxiation from drowning of the baby in its mother's breast'. I think when investigating the cause of such a sudden death this point should also be kept in mind.

Yours faithfully,
S. N. RAY.

P. O. GOPALPUR,
Dist. MYMENSINGH,
21st February, 1950.

CLINICAL HYDROPHOBIA WITHOUT CONTACT WITH RABIES TRANSMITTING ANIMAL

SIR,—The article by Dr. Deshmukh which appeared in the December issue of the *Indian Medical Gazette* (1949), recording no less than five cases of hydrophobia, none of which had a known source of infection, has been commented upon by you. Will you allow me to add further comments.

In the entire literature on rabies, since Pasteur's day, there have been recorded less than half a dozen cases of infection of an 'indirect' nature. That is to say less than six persons not bitten or licked by a rabid animal are known to have acquired hydrophobia from contaminated material. Even in these most exceptional, and possibly doubtful cases, the source of infection has been saliva of a known animal contaminating a known object. For example, Prausnitz (1926) records the case of a woman who developed hydrophobia as a result of biting off the thread she had used in sewing a garment torn by a rabid dog. Such cases, however, are so few that it may be claimed that they have no practical bearing on the problem of rabies. Infection from an absolutely unknown source is still more uncommon, and, so far as I am aware, there has only been one such case ever recorded—that of Glausman (1928). One, therefore, is justified in expressing some surprise that any doctor should be able to describe five such cases occurring in his own practice. Dr. Deshmukh's suggestion that the virus of rabies may remain attenuated in drinking water, and so cause infection through abrasions in the mouth,

would not be accepted as a common cause of hydrophobia by any rabies research worker, for all experienced workers can testify to the fact that many untreated control animals escape infection even when a thick emulsion of street virus is injected intramuscularly. Moreover, the practice, more common than is perhaps realized, of dogs licking plates and dishes without resultant 'indirect' infection rules out any probability of water-borne rabies. Also, to subscribe to the author's view, that a rabid dog has contaminated the water supply, in itself suggests that members of the household have been subjected to other, far more probable sources of infection: for obviously the rabid dog would have to enter the house and find the water supply to be able to contaminate it. Such deliberate behaviour would be strange on the part of any stray rabid animal which normally would not enter a house without attacking the inmates nor leave the house in so furtive a manner as to be unobserved.

In an addendum Dr. Deshmukh seizes on rats as an alternative source of infection and states 'After the above was written the author read with interest "rats are susceptible to rabies, and theoretically constitute a possible reservoir and source of infection" (Willmoth, 1949)'. Dr. Deshmukh wrongly attributes the statement to Willmoth, for the words quoted by him were given by an anonymous writer in reply to a query by Dr. Leonard who had asked the Editor of the *Journal of the American Medical Association* if it was necessary to give antirabic treatment to persons bitten by rats. This query was referred to two experts one of whom replied unequivocally 'As rats do not cause rabies there is no reason for using rabies vaccine in such cases. It is well known that rabies vaccine by itself in some cases may cause undesirable results'. The second expert replied in the words quoted by Dr. Deshmukh and added to this statement—'rabies in rats (in nature) is minimal'. The fact that rats 'are susceptible and theoretically constitute a possible reservoir of rabies' is undeniable, for this is true of every warm-blooded creature, including birds. It should, however, be borne in mind that rabies infection in rats 'is minimal', because a rabid dog or jackal, cat or mongoose, will not hunt or pursue a rat, and because a rat bitten by any such animal is likely to be killed outright.

So far as India is concerned there has never yet been a single case recorded of hydrophobia following the bite of a rat.

The public need have no fear of idiopathic hydrophobia, or of sudden epidemics of water-borne or rat-borne rabies, despite the claim to the unique experience of witnessing no less than five cases of hydrophobia of unknown origin.

Yours faithfully,
A. G. BROOKS,

Secretary,
Rabies Advisory Committee,
Indian Research Fund Association.

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M.D. AND M.S., BOMBAY

SIR,—I have to request you to publish the following in your esteemed Journal:—

It has been a great shock to the student world to hear the decision of the Medical Faculty of the Uni-

versity of Bombay to lengthen the course of M.D. and M.S. degrees from two years to three years.

I cannot understand why the Medical Faculty has arrived at the decision to lengthen the course for these examinations. Is it because the professors cannot cover the course in two years or is it because the students are not able to cope with the requirements within that period? The students are not incapable of completing the M.D., M.S. course within two years, if proper arrangements are made to coach them as is done in other countries. Then the other reason seems to be that the professors are either unable to devote sufficient time to cover the courses and impart instruction to students within the limit of two years or that they are not competent enough to train the students in that period. If such is the case, it is unreasonable to impose a further burden on the students in respect of time, energy and money.

As no university either in India or the United Kingdom has this particular course so lengthy, it is clearly necessary for the Faculty to reconsider the decision and to let the term remain two years as before so that medical men may be able to give the benefit of their knowledge and experience for the good of humanity for at least a year more.

If the Faculty does not do this, the question arises whether it will ban the recognition of qualifications obtained elsewhere in less than the period of three years after graduation.

Yours faithfully,
SHIRIN KHAMBATTA.

AVA MANSION,
TAMBO ROAD,
BOMBAY.

Service Notes

APPOINTMENTS AND TRANSFERS

DR. K. C. K. E. RAJA, Director-General of Health Services, was placed on deputation to Switzerland from the afternoon of the 30th November, 1949 to the 22nd December, 1949.

Dr. K. V. Venkataraman, Officer on Special Duty in the Office of the Serologist and Chemical Examiner to the Government of India, Calcutta, is appointed as Serologist and Chemical Examiner to the Government of India, Calcutta, with effect from the afternoon of the 31st December, 1949, *vice* Lieutenant-Colonel S. D. S. Grevail.

Mr. S. K. Mustafi, Depot Manager, Medical Store Depot, Raipur, is transferred as Depot Manager, Medical Store Depot, Calcutta, with effect from the afternoon of the 9th January, 1950.

Mr. P. C. Kapur, Depot Manager, Medical Store Depot, Calcutta, is transferred as Depot Manager, Medical Store Depot, Karnal, with effect from the afternoon of 20th January, 1950.

Mr. M. G. Pandit, Deputy Assistant Director-General (Medical Stores), Medical Stores Depot, Calcutta, is transferred as Deputy Assistant Director-General (Medical Stores), Medical Store Depot, Madras, with effect from the forenoon of 9th February, 1950.

LEAVE

Dr. Dharmendra, Officer-in-charge, Leprosy Inquiry at the School of Tropical Medicine, Calcutta, on foreign service under the Indian Research Fund Association, was granted earned leave for 42 days with effect from the 8th October, 1949, and to prefix

Sunday the 25th September, 1949, and the Punjab holidays from the 26th September to the 7th October, 1949. His services were replaced at the disposal of the Directorate-General of Health Services for the period of the leave.

Mr. S. C. Batra, Officer on Special Duty (Health Education) in the Directorate-General of Health Services, was granted earned leave for 55 days with effect from the 2nd November, 1949.

PROMOTION

The undermentioned officer of the late Indian Medical Service is advanced to the List of Special Selected Lieutenant-Colonels :—

Lieutenant-Colonel G. R. Oberai. Dated 1st June, 1946.

RETIREMENTS

The undermentioned officers of the late Indian Medical Service (Civil) have been permitted to retire with effect from the dates shown against their names :—

Lieutenant-Colonel G. D. Malhotra. Dated 3rd July, 1948.

Lieutenant-Colonel S. Annaswami. Dated 26th December, 1949.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints *gratis*; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

The preparation of reprints entails rearranging the type, so that there is often a delay of a month or more, after the publication of the *Gazette*, before the reprints are ready. If reprints are not received within two months of publication of the *Gazette*, contributors should write to the Publishers.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

CONTENTS

	Page		Page
ORIGINAL ARTICLES		An Unusual Case of Elephantiasis	
Perionychia due to Monilia Infection.		Buttocks. <i>By Susil Kumar Bhattacharjee, M.B. (Cal.), B.M.S.</i>	158
<i>By D. Panja and A. K. Banerjee</i>	137		
An Observation on Preserved Ova of		EDITORIAL	
Ascaris Lumbricoides. <i>By A. Sen-</i>		The Hormones	159
<i>gupta, M.B., D.T.M., and Sanatkumar</i>			
<i>Mitra, M.B.</i>	138		
An Unusual Case of Post-kala-azar		SPECIAL ARTICLE	
Dermal Leishmaniasis. <i>By P. C. Sen</i>		Treatment of Epidemic Dropsy. <i>By</i>	
<i>Gupta, M.B. (Cal.), D. Panja, M.B.</i>		<i>R. N. Chaudhuri and N. K. Chakravarty</i>	165
<i>(Cal.), and A. K. Banerjee, M.B., D.T.M.</i>	138		
Studies on Plasma Proteins. I. Kala-		MEDICAL NEWS	
azar. <i>By H. Chakravarti, M.D. (Cal.)</i>	141	C. A. BENTLEY, C.I.E., M.D., D.P.H.	172
Malformations of the Foetus (Monsters).		WORLD HEALTH DAY, 7TH APRIL, 1950.	
A report of five cases. <i>By B. P. Tribedi,</i>		PLAGUE CAN BE ERADICATED. BY THE	
<i>M.B. (Cal.), D.B. (Lond.), F.N.I., and</i>		EXPERT ADVISER ON PLAGUE AT THE S.-E.	
<i>A. R. Roy, M.B., Captain, I.M.S.</i>		ASIA REGIONAL OFFICE OF W.H.O.	173
<i>(late)</i>	144	BABIES' 'SUFFOCATION' OFTEN WRONG DIAG-	
Separation of Lids by Lid Sutures in		NOSIS	173
Cataract Extraction. Report on fifty		INTERNATIONAL SOCIETY OF HAEMATOLOGY—	
cases. <i>By B. K. Dhir, M.S. (Ophthal.),</i>		CAMBRIDGE CONGRESS—21ST-26TH	
<i>D.O.M.S. (Lond.)</i>	149	AUGUST, 1950	174
Treatment of Infantile Cirrhosis of the		MEDICAL PHOTOGRAPHY	174
Liver. <i>By P. Krishna Rao, B.Sc., M.B.,</i>		REGISTRATION OF DENTISTS : TIME LIMIT TO	
<i>B.S., D.T.M. & H. (Eng.), F.A.S.C.</i>	150	BE EXTENDED	174
Chloromycetin in Typhoid and Para-		PRESIDENT TO OPEN FUEL RESEARCH INSTI-	
typhoid Fever. <i>By Rudolf Treu, M.D.</i>		TUTE : THIRD IN CHAIN OF 11 NATIONAL	
<i>(Cologne), L.R.C.P. & S. (Edin.)</i>	154	LABORATORIES. PHYSICAL AND CHEMICAL	
		SURVEY OF COALS	175
A MIRROR OF HOSPITAL PRACTICE		INDIA AWARDS SEVENTY SCHOLARSHIPS	176
Abscess Breast. <i>By A. G. Chacko, B.A.,</i>		LABELLING PROVISIONS UNDER DRUGS ACT :	
<i>M.B., B.S.</i>	157	RIGID ENFORCEMENT TO START IN JULY	176

(Continued on page 136)

CONTENTS—(Continued from page 135)

	Page		Page
HEALTH MACHINE INVENTION CURES DIVERSE COMPLAINTS. AUSTRALIAN APPARATUS EXPEDITES BLOOD CIRCULATION AND TONES UP SYSTEM. <i>By Charles Lynch</i>	176	HEALED SUBACUTE BACTERIAL ENDOCARDITIS: A NEW ENTITY. <i>By S. R. Kaplan et al. (Journal of the American Medical Association, Vol. 141, 10th September, 1949, p. 114)</i> ..	182
THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL	177	REFRACTORY AMOEBIC ABSCESS OF THE LIVER TREATED WITH CHLOROQUINE. <i>By J. Emmett (Journal of the American Medical Association, Vol. 141, 3rd September, 1949, p. 22)</i>	182
FIFTY YEARS AGO			
THE ANNUAL MEETING OF THE BRITISH MEDICAL ASSOCIATION (<i>Indian Medical Gazette, April 1900, Vol. 35, p. 143</i>) ..	177		
CURRENT TOPICS, ETC.			
AUREOMYCIN IN INFECTIONS OF THE URINARY TRACT. <i>By J. R. Franklin (Ohio State Medical Journal, Vol. 45, May 1949, p. 460, as abstracted in the International Medical Digest, Vol. 55, September 1949, p. 152)</i>	179	TEXTBOOK OF OPHTHALMOLOGY. <i>By Sir W. Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Ph.D., M.D., Ch.B., F.R.C.S., etc. Volume IV. 1949</i>	182
SURDELTOID BURSTITIS. <i>By P. E. Wylie (Military Surgeon, Vol. 105, September 1949, p. 237)</i>	179	SEX AND ITS MYSTERIES. <i>By G. R. Scott, F.Z.S., F.Ph.S. (Eng.). 1948</i>	183
SOMATIC MOVEMENTS OF THE PREMATURELY BORN FÆTUS—FILM DEMONSTRATION <i>By I. Mackenzie (Proceedings of the Royal Society of Medicine, Vol. 42, November 1949, p. 877)</i>	180	FORENSIC MEDICINE: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS. <i>By Sir Sydney Smith, C.B.E., M.D. (Edin.), F.R.C.P. (Edin.), D.P.H., and Frederick Smith Fiddlers, O.B.E., M.D. Ninth Edition. 1949</i>	183
A SIMPLE NEW STAIN FOR INTESTINAL PROTOZOA. <i>By M. I. E. Kordy (Journal of the Royal Egyptian Medical Association, Vol. 32, May 1949, p. 426)</i> ..	181	BOOKS RECEIVED .. 183	
FOLIC ACID AND NEUROLOGIC CHANGES IN PERNICIOUS ANEMIA (<i>Canadian Medical Association Journal, Vol. 61, August 1949, p. 172</i>)	181	ABSTRACTS FROM REPORTS	
THE CYTOLOGICAL DIAGNOSIS OF MALIGNANT CELLS IN VARIOUS BODY FLUIDS. <i>By H. E. Taylor and W. J. Thompson (Canadian Medical Association Journal, Vol. 61, October 1949, p. 413)</i> ..	182	ANNUAL REPORT ON THE HEALTH OF THE ARMY IN INDIA FOR THE YEAR 1947. PUBLICATION No. 29393/AG/ORG/IASO/PERS (MED.), A.G. BRANCH. PRINTED BY THE GOVERNMENT OF INDIA PRESS, NEW DELHI, FOR THE MINISTRY OF DEFENCE DEPARTMENT, GOVERNMENT OF INDIA, NEW DELHI	
ANY QUESTIONS			
		PRIMARY AND RELAPSING MALARIA ..	184

Original Articles

PERIONYCHIA DUE TO MONILIA INFECTION

By D. PANJA

Officer-in-Charge

and

A. K. BANERJEE

Assistant Research Officer

Study of monilia infection of the skin and adjacent mucous membrane, under the Indian Research Fund Association, School of Tropical Medicine, Calcutta

THE yeast-like fungus *monilia* is widely distributed in nature. It has been found in saprophytic state in man on the skin and mucous membrane of mouth, genitalia and respiratory and gastro-intestinal tracts. Various members of the genus *monilia* have been shown to be the causative agents of a number of pathological conditions affecting the skin and the mucous membranes. It is generally believed that some members of *monilia* group, frequently present as saprophyte in man, may under favourable conditions assume parasitic habits and become pathogenic giving rise to diseases of skin and mucous membranes.

Perionychia caused by infection with *monilia* is not very uncommon. It is usually found in adults and old people and rarely seen among the children. The majority of the patients suffering from this condition are females belonging to the middle and the poorer classes whose normal duties entail frequent washing of hands in water. This condition has therefore been commonly observed among the females who perform the routine domestic work, among labourers, cultivators, gardeners, and those dealing with sugar-candy, fruits, vegetables, etc. History of long duration with practically no improvement with treatment is usually obtained. The patients are usually seen with painful swelling of the soft tissues surrounding one or more nails mostly of the fingers of the hands, thumb and middle finger of the right hand being commonly involved. In some cases there may be associated discoloration and deformity of the nails to a varying degree. The affected nails are usually depressed and from the base of the nail a thick purulent material can be expressed out. The commonest and the most troublesome complaint is the difficulty in carrying out their normal duties, because the pain and irritation become more pronounced when foreign material and sometimes even water get inside the nail folds.

Recently we studied a series of 35 cases of perionychia at the skin clinic of the School of Tropical Medicine. In 23 of these 35 cases

monilia could be isolated. These positive cases include 4 adult males and 19 females.

Illustrative case notes

(1) Female, aged 44 years. Maidservant.

About 6 years ago she developed painful oedematous condition of the tissues surrounding the nail of the right index finger. The base of the nail was first affected; gradually the diseased process extended round the nail towards the tip of the finger. This condition rapidly affected the fingers and thumbs of both hands so that within 3 months all the digits were involved.

General history of the previous illness and the systematic examination of the patient revealed nothing significant. On local examination moderate inflammatory swelling of the surrounding parts of the finger nails of both hands with associated pain and tenderness was detected. The pain and swelling were most marked near the base of the nail. Seropurulent discharge from the nail fold was seen on pressing the inflamed tissue near the lunula of all the fingers excepting the thumb and little finger of the left hand. All the nails of the affected fingers were deformed and were found to have lost the normal smooth and glossy appearance, the changes being more marked in the right hand (figure 1, plate XXII). These nail affections caused discomfort in carrying out her normal domestic duties.

(2) Female, aged 30 years. Came from a middle-class family.

The patient complained of pain and swelling^{*} surrounding the nails of the right thumb and middle finger of the left hand. The affected nails showed discoloration and disfigurement. Lesion on the thumb appeared about 2½ years ago after which similar condition developed on the middle finger in course of 2 to 3 months.

On examination tenderness and swelling of the soft tissue surrounding the nails of the affected fingers were found. There was no discharge from any of the lesions. The nails were blackish in colour, thick, rough and marked by transverse furrows. The distal parts of the nails were elevated and the spaces between nail beds and nails were filled with necrosed tissue (figure 2, plate XXII). The condition was painful enough to interfere with her normal domestic duties and other works.

(3) Male, aged 30 years. Vegetable dealer.

He said that for the last 7 years he had been suffering from painful swelling of the soft parts surrounding the nails of the middle, ring, and little fingers and thumb of the right hand, middle finger of the left hand (figure 3, plate XXII) and great and third toes of the right foot. He tried different medicines for a long time but with no appreciable result.

The condition of the nails and toes used to get worse during the rainy season; oedema, ulceration, seropurulent discharge, burning and

pain being the chief manifestations. These symptoms greatly interfered with his work and even compelled him to take to bed on several occasions.

Mycological study

Microscopical examination of the direct smear from the lesions of perionychia did not reveal any clue regarding the causative organism (as the monilia could not be detected in all cases) except some cocci which might be a constant factor in an open ulcerated surface of skin. Cultural examination was done in each case. The diseased part had been soaked with antiseptic lotion for 24 to 72 hours to make the surface clean and partly free from coccal infection. The primary cultures were made on Sabourraud's maltose peptone agar, glucose agar and ordinary agar media; the former two media are most suitable for the growth of the organism. The growth of monilia colonies was detected in 48 to 72 hours, though it was noticed even in 24 hours in a few cases. The subcultures were rapidly grown in 24 hours either at 37°C. or at room temperature under aerobic conditions. The colonies were round or oval in shape and were glossy white or cream coloured in appearance.

For the identification of the species of monilia recovered from the cases, biochemical reactions were studied.

The following carbohydrates were used—dextrose, levulose, maltose, galactose, saccharose, lactose, mannitol, dextrin, raffinose, arabinose, inulin, glycerine, xylose, and also milk for clotting.

Species of monilia identified so far are :

<i>M. pinoyi</i>	11
<i>M. nabarroii</i>	5
<i>M. bronchialis</i>	7

The commonest species *pinoyi* ferments dextrose, levulose and maltose, whereas *albicans*, the commonest in other countries, ferments dextrose, levulose, maltose and galactose.

Summary

(1) In our cases of perionychia the causative organism was found to be monilia due to its constant presence on repeated culture of the infected materials. On primary culture a pure growth of monilia colonies was present in many cases.

(2) In this series of cases of perionychia, *Monilia pinoyi* was found to be the commonest organism causing the lesions; whereas in other countries *M. albicans* is the most prevalent organism.

(3) The perionychia is more common in females than in males.

(4) It is a very resistant and troublesome disease causing disability to labourers, cultivators, gardeners, housewives and those dealing with sugar-candy, vegetables, fruits, etc.

The treatment of this condition will be discussed in the next article of this series.

AN OBSERVATION ON PRESERVED OVA OF ASCARIS LUMBRICOIDES

By A. SENGUPTA, M.B., D.T.M.

Assistant Professor of Pathology
and

SANATKUMAR MITRA, M.B.

Demonstrator of Pathology
Lake Medical College, Calcutta

RECENTLY in the class when a preserved specimen of faeces was given for examination, we observed that in several ascaris ova a small larva was wriggling within the shell. This was also noted by our colleagues Dr. Bag and Dr. Dutt and several students. As we watched, an area of the shell of one ovum gave way—opening up as if on hinges and the larva wriggled out. As soon as the larva came out it died. After a couple of minutes the whole egg-shell crumbled. In several other smears of the specimen larvae were seen, apparently dead, half in and half out of the shell. We have not seen this phenomenon with ascaris ova before. My (A. S.) experience in examination of preserved faeces is however very limited. The specimen was preserved by formalin method three weeks previously. (Faeces diluted with water, mixed with equal quantity of hot 10 per cent formalin, allowed to stand for a few hours, supernatant fluid decanted off and replaced by 5 per cent formalin, and kept in stoppered bottles.) Before giving the specimen to the class the supernatant formalin solution was decanted off and replaced by normal saline.

The ova had therefore remained viable even after the treatment with formalin as above. The albuminous coat of the shell acted as an effective barrier against the penetration of formalin. The amount of formalin present even after replacement by normal saline was however potent enough to kill the larvae instantly as soon as they came out of the shell.

We thank the Principal and the Professor of Pathology, Lake Medical College, Calcutta, for their kind permission to send this communication for publication.

AN UNUSUAL CASE OF POST-KALA-AZAR DERMAL LEISHMANIASIS

By P. C. SEN GUPTA, M.B. (Cal.)

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Research Department

(From the Calcutta School of Tropical Medicine)

THE commonest forms of post-kala-azar dermal leishmaniasis are the hypo-pigmented

macule, the butterfly erythema and the nodule. The other varieties of lesions that are occasionally seen are the verrucose, papillomatous, hypertrophic and xanthoma types. Perionychial induration and ichthyotic condition of the skin due to this disease have also been described. In this paper we present the notes of a case of post-kala-azar dermal leishmaniasis presenting some unusual features, along with the results of histological and other laboratory investigations and then proceed to discuss the findings in the light of the present knowledge relating to the clinical features and histopathology of post-kala-azar dermal leishmaniasis.

CASE NOTE

A K B, an Indian male, aged 18 years, was admitted into the hospital of the Calcutta School of Tropical Medicine on the 20th October, 1949, for post-kala-azar dermal leishmaniasis.

About ten years ago the patient suffered from prolonged pyrexia that was diagnosed as kala-azar and was treated with 20 intravenous injections (? urea stibamine). About a year and a half after the cure of kala-azar, the patient noticed the appearance of partially depigmented areas first on the face, then on the trunk and subsequently on the extremities. The nodular swellings appeared first on the face about the time of appearance of the depigmented patches on the trunk, the raised eruptions on the body appeared subsequently. He was treated for dermal leishmanoid about seven years ago with 23 intravenous injections (? antimonials). But the lesions were not markedly influenced by this treatment.

The patient first noticed the depressed scars on his face about a year and a half after the completion of this course of intravenous injections. These appeared on the areas where he had developed nodular type of lesions.

Except for an attack of pneumonia four years previous to his admission into the hospital and occasional attacks of diarrhoea with passage of mucus, the patient did not suffer from any other diseases since the attack of kala-azar. But he occasionally complained of abdominal pain and acidity and after his admission into the hospital he showed symptoms of internal piles.

On examination the cutaneous lesions were (figures 1, 2 and 3, plates XXIII and XXIV) hypo-pigmented patches almost all over the body extending over the face, trunk, the upper and the lower extremities; there was a hypo-pigmented patch on the mucous membrane of the hard palate.

Nodular type of lesions slightly raised above the surface of the skin, on the trunk, the chin and the external genitals; most of these lesions showed irregular superficial thinning of the skin to an almost thin shiny tissue-paper appearance; the pigmentation was uneven in the different parts of each of these areas, the colour varying from hypo-pigmentation to normal colour, there was no ulceration anywhere.

Depressed scars on the face, situated round the mouth, on the cheek, on the eyelids near both canthi except the inner canthus of the left eye; these scars were darker in colour than the surrounding skin; there was slight thickening of the eyelids.

Slight ichthyotic changes of the skin were noticed over the forearms and legs.

General examination showed slight enlargement of the liver and tenderness over the right iliac, epigastric and left hypochondriac regions. Proctoscopy revealed internal piles. No other abnormality was detected.

Laboratory tests

Hæmoglobin 12.4 gm. per 100 cc. of blood; RBC 4.95 million per c.mm.; WBC 8.9 thousand per c.mm.; neutrophils 52, lymphocytes 29, monocytes 5 and eosinophils 14 per cent of WBC.

Wassermann test: negative.

Kahn test: negative.

Mantoux test: negative in 1:10,000.

Complement fixation test for kala-azar: 'doubtful' reaction.

Smear from a nodular lesion: L.D. bodies present.

Bacteriological examination for leprosy: no acid-fast bacilli seen.

Urine examination: no abnormality.

Fæces: vegetative and cystic forms of *E. histolytica*, cysts of *Giardia intestinalis*, and *Trichomonas hominis* were found.

Skiagram of the chest: no signs of tuberculous disease.

Barium meal skiagraphy of the gastro-intestinal tract: duodenal ulcer present. Signs suggestive of colitis affecting proximal part of the descending colon also present.

Histological examination of the cutaneous lesion

The biopsy material collected under local anaesthesia consisted of a nodular type of lesion showing irregular thinning of the skin. The specimen was fixed in Zenker's fluid, dehydrated in the usual manner and embedded in paraffin. The sections were stained with (a) M. N. De's iron hæmatoxylin and eosin stain, (b) Van Gieson's stain, (c) Giemsa's stain according to the technique described by Shortt and Cooper (1948), and Ziehl-Neelsen stain.

The histological changes noted were as follows:—

The epidermis.—The epidermis was intact throughout. There were some areas showing thickening of the stratum corneum particularly where the granulation tissue in the dermis was not close to the epidermis. There was no parakeratosis. The granular layer consisted of one or two layers of cells. The rete cones were flattened out in many areas. The rete malpighii was markedly thinned out being reduced to one to three layers of cells only. The basal layer was composed of one and in places two layers of cells containing pigment. In areas where the granulation tissue was encroaching on the epidermis, the pigment content was distinctly less.

The dermis.—The papillae were flattened in many areas. Collections of granulation tissue were seen in the dermis in its superficial or papillary layer and the deeper reticular layer, in relation to the blood vessels, hair follicles, sweat and sebaceous glands.

The granulation tissue was not equally vascular in different areas. In some the capillaries were abundant and filled with blood while in others the marked feature was the cellular proliferation with relatively less

vascularity. The cells in the granuloma were large mononuclear histiocytes, lymphocytes, plasma cells, a few eosinophils and fibroblasts. Polymorphonuclear neutrophil leucocytes were inconspicuous. The cytoplasm of the cells about the centre of an island of cellular proliferation was pale and the nuclei were vesicular: the cells were larger (? reticular cells) than the more differentiated cells in the periphery, *viz.* the histiocytes, lymphocytes and plasma cells (figure 4, plate XXV). Pigment containing cells (chromatophores, and ? detached cells from the basal layer of the epidermis) were seen in the superficial region of the dermis.

An area of granulation tissue containing a large collection of giant cells of the Langhans' type was seen situated close to the epidermis. There were no leishmania or acid-fast bacilli in this focus. There was some granular homogeneous degenerated material about the centre of this collection of giant cells. The other cells in this focus were the histiocytes, lymphocytes and a few plasma cells. The overlying epidermis was greatly thinned out and the basal layer contained much less pigment than the adjacent areas. There were bands of fibrous tissue lying internal to and also extending through this area (figure 5, plate XXV).

Histiocytes containing Leishman-Donovan bodies were found, but the number of such cells was not large. These were found in some areas of cellular proliferation in the depth of the lesion and near the periphery of the affected portion of the skin.

With Van Gieson's stain marked proliferation of the collagen fibres was noted in the layers of the dermis. Strands of these fibres were seen to be extending through and around the areas of cellular granulation tissue. Interlacing bundles of coarse collagen fibres were seen in the papillary layer of the dermis as well as in the deeper reticular layer. In areas collagen fibres were found to be extending between the cells of the basal and malpighian layers of the epidermis along with granulation tissue.

The blood vessels did not show any change except for those embedded in dense fibrous network. The latter showed some degree of constriction and thickening.

Discussion

It will be evident from the notes of this case that the patient had kala-azar about ten years ago and that the first lesions of post-kala-azar dermal leishmaniasis appeared about a year and a half after the cure of kala-azar. The patient had some treatment for the dermal condition about seven years ago but this did not lead to any immediate results. About a year and a half later, the patient noticed the appearance of depressed scars where there had been nodular lesions on the face.

It is well known that unlike oriental sore, post-kala-azar dermal leishmaniasis does not usually go on to ulceration and the lesions heal without any scarring. The skin is as a rule quite normal after the disappearance of the lesions which are characterized by overgrowth of tissue, *e.g.* the nodular type. Thus the development of depressed scars at the site of nodular lesions and the irregular tissue paper-like thinning of the skin over areas of nodular lesions were unusual features for post-kala-azar dermal leishmaniasis. Also the hypo-pigmented patch on the mucous membrane of the hard palate was a rare condition.

The presence of atrophic scars and shiny appearance of the skin over the nodular lesions suggested the possibility of other co-existing infections. Leprosy was excluded by clinical and bacteriological examination, and syphilis by negative Wassermann and Kahn tests. There were no signs of tuberculous disease and the Mantoux test was negative. Also no acid-fast bacilli were found on histological examination. On the other hand, smears from the nodular lesions showed Leishman-Donovan bodies.

Histological examination of the biopsy material yielded interesting findings.

Excessive amounts of fibrous tissue were found in the layers of the dermis and coarse bundles of collagen were found in the papillary layer where normally fine strands only are seen. This was apparently responsible for the production of the depressed scars. The marked thinning of the epidermis by the pressure of the underlying granulation tissue and the extension of granulation tissue and collagen fibres into the layers of the epidermis had apparently led to the irregular thinning of the skin over the nodular lesions. Such changes are however not usual in post-kala-azar dermal leishmaniasis in which fibroblasts are few as a rule and the lesions heal without any fibrosis and scarring.

The presence of a focus of collection of giant cells of the Langhans' type in an area of granulation tissue situated in the papillary layer of the dermis was also an unusual feature. There was some degenerated material about the centre of this focus. No leishmania or other organisms were found in or near this collection of giant cells. Though the presence of multinucleated giant cells containing many leishmania is not very uncommon in post-kala-azar dermal leishmaniasis, there is no record of the presence of what is essentially a tuberculoid focus in this condition. It is however well known that in recurrent oriental sore, histological picture closely resembles that of cutaneous tuberculosis.

The development of a tuberculoid focus in this case can be compared to the causation in neural leprosy of tuberculoid lesion that heals by fibrosis and at times leads to the formation of neural abscesses. It is possible that the excessive fibrosis seen in this case was provoked

1. Early kala-azar, who were admitted in the hospital as typhoid cases but were subsequently diagnosed to be kala-azar (4 cases).

2. Spleen enlarged up to 2 inches below costal margin (8 cases).

3. Spleen enlarged under 4 inches below costal margin (21 cases).

4. Spleen enlarged 4 inches above or below the costal margin (24 cases).

Sizes of the spleen mentioned above are applicable to an adult only and due consideration was given in cases of children. Cases with cancrum oris were included in group 4 irrespective of the size of the spleen. Comparative picture of the plasma protein changes in these different groups appears in figure 2; the range, mean and

changes are not so remarkable in these cases in the beginning but as the disease progresses the usual changes of kala-azar become apparent.

Variations from the usual pattern

1. *Malnutrition*.—It is well known that malnutrition vitiates the usual picture observed in various diseases and this is true in kala-azar cases as well. In a case which has been included under group 4 there were marked clinical signs of malnutrition including angular stomatitis, sore tongue, rough skin, oedema and moderate anaemia (8.7 gm. per cent of Hb.). Plasma protein was 4.8 gm. per cent, albumin 2.0 and globulin 2.8 gm. per cent. This is contrary to the usual finding observed in this group and seems to be the direct result of malnutrition and the underlying kala-azar having little influence in producing the usual change.

2. *Anaemia*.—Varying degree of anaemia is associated always with kala-azar and no relation however exists with the plasma protein changes; but in presence of grave anaemia the usual picture of plasma protein changes is very much altered as will be evident from table III.

The albumin and total protein tend to be low whereas the globulin may or may not rise at all.

3. *Oedema and/or ascites*.—This is frequently found in late kala-azar cases. In the present series this was noticed in a number of them and the plasma proteins are tabulated in table IV.

Except in the third case (table IV) where there was marked malnutrition no significant difference can be observed in these cases as distinct from the others in the same group. Marked albumin depression was found in all of them but the colloidal osmotic pressure is not very much lowered as will be evident from the figures calculated by Govaert's formula. This is due to compensatory rise in the globulin fraction. In one case only the oedema may be explained by the associated severe anaemia and in two cases there were signs suggesting cirrhotic changes in the liver which may explain the ascites.

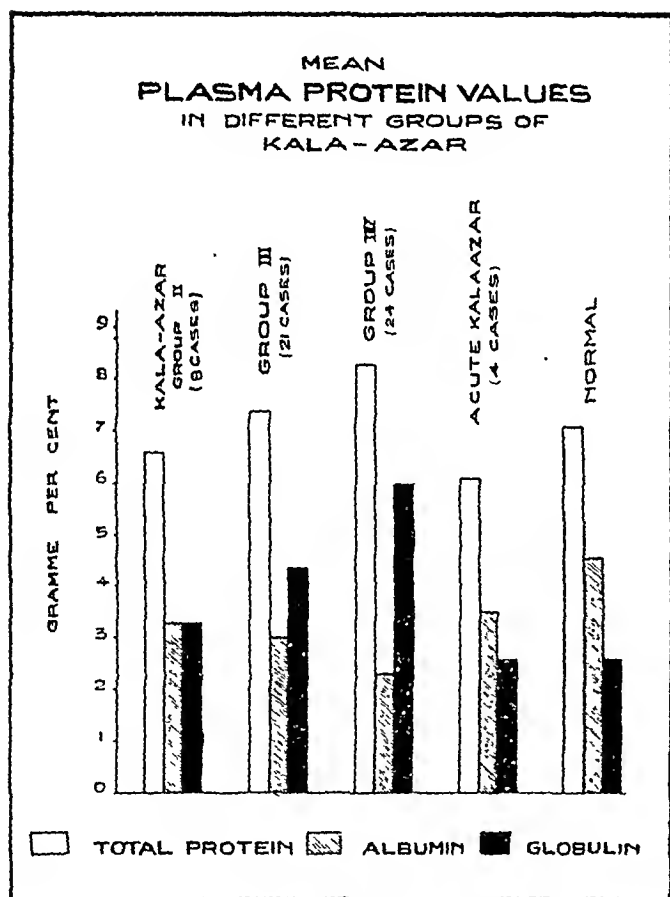


Fig. 2.

standard variation being given in table I. It will appear that although there are individual variations, there is also a group characteristic in each of them. The hyperproteinæmia with hyperglobulinæmia tends to be more intensified as the disease progresses. The group of early cases of kala-azar deserves special consideration.

Early kala-azar.—These four cases were admitted as typhoid fever and the plasma protein changes were observed for that disease; but subsequently they proved to be kala-azar and again plasma proteins were estimated after the diagnosis. The results are interesting and appear in table II. It will be evident that the

Discussion

In general, the present observations agree fairly well with those of previous workers with only a few notable variations. Thus in early kala-azar the changes observed are more like those of enteric fever. As the disease progresses the hyperglobulinæmia develops and, broadly speaking, splenic enlargement was found to be an index of such changes but in presence of malnutrition or severe anaemia they do not develop. In kala-azar voracious appetite is probably responsible for absence of any signs of chronic malnutrition but for any reason if there is any deficiency of food intake, particularly proteins, hypoproteinæmia may manifest itself.

TABLE I

			Total gm. per cent	Albumin, gm. per cent	Globulin, gm. per cent	A/G X : 1
Group 1	Range	..	5.8-7.2	2.8-4.1	2.7-3.9	0.8-1.4
acute kala-azar	Mean	..	6.63	3.27	3.36	1.0
(4 cases).	S.D. ±	..	0.46	0.44	0.39	0.20
	Range	..	4.8-9.6	1.7-4.4	2.8-5.3	0.2-1.0
Group 2	Mean	..	7.35	2.91	1.41	0.69
(8 cases).	S.D. ±	..	1.11	0.66	1.08	0.20
	Range	..	5.5-10.6	1.4-1.0	3.6-8.7	0.2-0.9
Group 3	Mean	..	9.32	2.31	5.97	0.42
(21 cases).	S.D. ±	..	1.19	0.62	1.24	0.17
	Range	..	5.5-6.8	3.1-1.2	2.2-3.0	1.1-1.6
Group 4	Mean	..	6.08	3.45	2.62	1.35
(24 cases).	S.D. ±	..	0.42	0.45	0.33	0.20
Normal	Range	..	6.2-8.0	3.9-5.5	2.0-3.3	1.5-2.4
(75 cases).	Mean	..	7.1	4.5	2.6	1.8
	S.D. ±	..	0.52	0.37	0.29	0.23

TABLE II

Cases	Days	PLASMA PROTEINS IN GM. PER CENT						A/G X : 1	
		Total		Albumin		Globulin			
		Before	After	Before	After	Before	After	Before	After
1	22	6.2	6.7	3.2	3.0	3.0	3.7	1.1	0.8
2	..	6.8	..	4.2	..	2.6	..	1.6	..
3	30	5.5	6.4	3.3	3.2	2.2	3.2	1.5	1.0
4	21	5.8	6.8	3.1	2.9	2.7	3.9	1.2	0.7
Mean (4 cases)	..	6.8	..	3.45	..	2.62	..	1.35	..
S.D. ±	0.41	..	0.45	..	0.33	..	0.20	..

N.B.—Before = On admission.

After = After diagnosis of kala-azar.

Days indicate difference between first and second observation.

TABLE III

Group of the case	Hb., gm. per cent	R.B.C. million per c.mm.	Total protein, gm. per cent	Albumin, gm. per cent	Globulin, gm. per cent	A/G X : 1
2	3.2	1.15	5.8	3.1	2.7	1.2
2	2.95	1.3	6.1	2.9	3.2	0.9
3	3.7	1.5	5.1	2.0	3.1	0.7
4	3.85	1.1	5.5	1.9	3.6	0.5

TABLE IV

Group of the case	Ascites	Edema	Total protein, gm. per cent	Albumin, gm. per cent	Globulin, gm. per cent	A/G	Osmotic pressure (Hg. of mm.)
4	0	+	7.5	1.9	5.6	0.34	18.4
4	+	+	9.8	1.8	8.0	0.2	21.2
4	+	+	4.8	2.0	2.8	0.7	15.0
3	+	+	7.9	1.7	6.2	0.3	18.0
3	0	+	6.8	2.6	4.2	0.6	..
1	+	+	6.1	2.9	3.2	0.9	19.5

Many of the serological tests of kala-azar like aldehyde test, antimony test and globulin precipitation test are due to quantitative or qualitative changes in the globulin fraction found in this disease and this explains why such tests are not so specific as they are frequently positive in other diseases like leprosy, chronic malaria, etc., where hyperglobulinæmia is also encountered. Increased rate of sedimentation of erythrocyte observed in kala-azar cases are also supposed to be due to increased globulin fraction (Newham and Martin, 1928). Higher incidence of positive Wassermann reaction in kala-azar is thought to be due to changes in the plasma protein pattern (Greval *et al.*, 1938).

The cause of such profound plasma protein changes is not clearly understood. Undoubtedly raised globulin is observed in most of the chronic infections but its degree in kala-azar is so great that it can only be paralleled by similar changes in a few chronic infections like tuberculosis and leprosy. This cannot be adequately explained by the 'host reaction' towards chronic infections only, nor is there any evidence that this is due to formation of antibodies alone. Ray (1927) suggested that the products of tissue degeneration are the source of increased globulin without any authentic proof however. In leprosy it has been suggested by Ross (1943) that the plasma protein changes observed can partly be explained by associated liver damage. Suggestion of hepatic dysfunction in kala-azar is also found from the study of morbid anatomy and other functional tests (Pai, 1941; Chakravarty *et al.*, 1949; Chaudhuri and Rai Chaudhuri, 1943; Napier and Sharma, 1933). It, therefore, seems probable that the extreme changes in the plasma protein may partly be due to concomitant hepatic dysfunction found in kala-azar. However, it must be emphasized that in any liver diseases such remarkable changes have not been observed. Moreover, changes are observed even in the early stages of the disease much before any remarkable variation in the liver function occurs.

Summary

1. In 57 unselected cases of kala-azar changes in the plasma protein pattern have been observed. In the early cases the changes are minimal but as the disease progresses the usual picture of hyperproteinæmia and hyperglobulinæmia appears and the degree of such change is proportional to the stage of the disease as judged by enlarged spleen.

2. In presence of malnutrition and severe anaemia the usual rise in globulin fraction does not occur. Oedema in kala-azar is not so much related to the lowered osmotic pressure of the plasma proteins.

3. It has been suggested that changes in the plasma protein pattern are due to both chronic infection and associated liver dysfunction in kala-azar.

My thanks are due to Professor R. N. Chaudhuri for his valuable guidance.

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MALFORMATIONS OF THE FŒTUS (MONSTERS)

A REPORT OF FIVE CASES

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MALFORMATION of the foetus is a curious phenomenon of which very little is known although from time to time various theories have been advanced to explain the condition. We are herewith reporting five such cases. The first two are examples of malformations involving one individual (single monster) and the last three are examples of malformations involving two individuals (duplicate monster). All of them were too malformed to be consistent with life and were either born dead, or died soon after.

CASE 1 (INTRA-AMNIOTIC AMPUTATION)

Clinical notes: No history of the case is available.

Description (figure 1, plate XVI)

The right lower extremity is missing from a little below the knee joint. The stump is narrowed down, and from its lower end projects a small piece of cartilaginous tissue. Right knee joint is enlarged and swollen. No other abnormality.

Skiagram (figure 2, plate XVI)

Right femur is normally developed. The shaft shows a fracture near the junction of the upper one-third and the lower two-thirds (might be due to manipulation during delivery). The lower end appears to be bifurcated and surrounding it is a big mass of tissue which has cast a shadow of nearly the same density as that of bone. Upper end of the tibia is not clearly seen (obliterated by the above mass). The small piece of shaft is seen to narrow down abruptly to the lower end of the stump from which projects the bent cartilaginous piece.

Dissection of the right knee joint showed that the patella was well formed. The patellar tendon was attached to the usual position. The knee joint was distended. On opening the joint it was found to contain thick creamy mass filling up the sacculations of the distended and thickened capsule. Articular cartilage at the lower end of femur was overgrown and projected outwards giving rise to the bifurcated appearance.

Other limbs and organs were normally developed and normally placed.

Discussion

This is an example of *monstra per defectum* (a single monster where all or part of an organ is missing).

The true mechanism of causation of such malformation is ill understood. Some consider that amniotic adhesions are responsible, resulting in fibrous bands (desmoplasts) which strangulate a particular organ leading to death of the part distal to strangulation. These bands leave their traces in the fetus as tags or scars. Ætiological factors concerned in the production of amniotic adhesions are: (i) local tissue injury, (ii) breakdown in the placental circulation due to injury to mother, (iii) syphilis, and (iv) infarction.

According to Sir Arthur Keith (1940) circulatory failure is the main factor. A local necrosis is produced by circulatory failure which may be placental in origin. The failure occurs along marginal areas where capillary formation is in progress. The amniotic adhesions are the result and not the cause of foetal malformation. In this particular case, however, no fibrous tag could be seen nor could any scar be demonstrated. As the missing part of the right lower limb was not found free in the amniotic cavity, presumably there was complete arrest of development of the lower part of the right leg and right foot, the mechanism of which is not very clear.

CASE 2 (ELEPHANT MONSTER)

Clinical notes: This monster was aborted after a few months' pregnancy due to high fever.

Description (figures 3 and 4, plates XXVI and XXVII)

The head, upper limb and trunk are malformed. There is only a pair of lower limbs connected with a short rudimentary trunk. Cranium is absent and is represented by a mass of skin which projects downwards in front bearing resemblance to the trunk of a baby elephant. Underneath the projection is a wide transverse opening, through which meconium is seen to come out (oral aperture). Eyes, ears, nose, etc., cannot be made out. The trunk is very short and rudimentary, and without any bones inside. There are multiple scars and tags on either side of its upper part. Umbilical cord is well formed and attached to the front aspect of the rudimentary trunk. On the back, at the lower part of the trunk is the anal aperture, overhung by a small tag of skin ($\frac{1}{2}$ inch long)—the rudimentary tail. There is no trace of the upper limbs. The lower limbs are rather well developed, each with two segments (thigh and leg), while from the lower extremities project rudimentary toes, three in the right and two in the left. Ankle and foot not differentiated. Left leg shows grooves (produced by scars) in the region of undifferentiated ankle, dorsum and sole of undifferentiated foot. There is a fibrous band as well in the latter situation. The right lower extremity shows grooves (produced by scars) in the region of undifferentiated ankle posteriorly, over the dorsum of the undifferentiated foot, in the middle of the leg, and a fibrous band on the medial aspect of the thigh. The genital organ is represented by a small nodule at the lower part of the trunk, between the two lower limbs.

Skiagram (figure 5, plate XXVII)

Cranium and trunk: An irregular mass in which no definite bones could be made out.

Limbs: No bones of upper limbs. Bones of the lower limbs, viz, the os innominata, femurs, tibiae, fibulae, and a few of the tarsal and metatarsal and phalangeal bones are well developed on either side.

Dissection

On opening up the trunk it was found that there was no differentiation into thorax and abdomen. The upper part was more or less solid, consisting of dense fibrous tissue. No trace of heart, lungs, pleural cavity, blood vessels or nerves could be seen. The lower part showed a small closed cavity (the peritoneal cavity), containing the alimentary canal, represented by a few, fairly well-developed coils (5 inches to 6 inches). The lumen of the alimentary canal had continuity with the oral aperture proximally, while the other end opened posteriorly at the lower part of the trunk at the

anal aperture. There was meconium in the intestinal canal, showing that it was not only fairly well developed but functioning. There was, however, no differentiation into mouth cavity, gullet, stomach and small and large intestines.

The head region (snout) showed a plate-like cartilaginous mass of irregular shape which did not conform to any recognized cranial bone. There was no trace of any brain matter anywhere.

Discussion

This is again an example of *monstra per defectum*, but of an extreme degree.

The malformations are the result of arrest of development at various stages due to amniotic adhesions. The scars and bands at the various sites, which on section show fibrous tissue, are reminiscent of old adhesions. The various processes which grow to form the face have been arrested at an early stage of development, leaving a wide cleft, separating the maxillary and nasal processes. The tip of the snout represents the cerebral membranes. The upper part represents the membranes of the thalamencephalon, the depressions represent the eyes. Underneath the snout is the transverse fissure of the face.

The multiple scars and tags on either side of the upper part of the trunk show that there was deficiency of circulation due to adhesions and resulting fibrosis, hence the arrest of development of organs beyond (Streeter's dysplasia) and no trace of upper limbs. In the trunk, the fibrous bands commence a little above the umbilical region and pass upwards towards the inner angle of the eye-pit, and other bands pass from hip to the top of the head passing just outside the eye-pit. There has been arrest of development of the trunk from a point a little above the umbilical region, the rest of the upper trunk, neck and head being represented by the mass of skin which resembles the snout of an elephant, and which has been dragged towards the umbilical cord by the fibrous bands.

The presence of multiple scars and bands (desmoplasts) in the grooves in the lower limbs bespeaks of the mechanism of arrest of development of feet and toes being the same as above.

The explanation given by Sir Arthur Keith (1940) for all such malformations may be summarized as follows: These are cases of 'Streeter's foetal dysplasia' of an extreme degree caused by amniotic bands of adhesions resulting in a 'local necrosis probably due to circulatory failure which may be placental in origin'.

The lesions become manifest at two stages of foetal development:

(i) Towards the end of the first month and (ii) towards the end of the second month. In this case, the stage at which the desmoplastic process started in the trunk was probably towards the

end of the first month, while those of the lower limbs were produced at a much later period.

CASE 3 (*DIPROSOPUS TETROPTHALMIUS*)

Clinical notes: No history of the case is available.

Description (figure 6, plate XXVII)

Anterior aspect: There are two heads fused in the middle line just behind the ears so that there are 4 auricles, 4 eyes, 2 noses, 2 chins and 2 openings of mouth, with a single neck. The trunk is single. There is one pair of upper and lower limbs in each. The penis is single and the scrotum contains two testicles. Umbilical cord is single. The cranium of each is extremely small and the cranial cavity is covered above by a thick piece of tissue (the dura mater).

Posterior aspect: The spinal column appears to be bifid. It runs downwards from between the two heads as two raised ridges to the level of the aë of the ileum.

Growth and development: Normal.

Skigram (figure 7, plate XXVIII)

The cranium of each is ill formed, and little or no cranial cavity (2 mm. by 12 mm.) is visible.

The vertebral column: Lower five vertebrae normal and single. The bodies of the rest of the vertebrae divided into two lateral halves, which, in the thoracic region, are wide apart and joined by the ribs laterally in each segment. The atlas and the odontoid process of the axis are very prominent. The vertebral canal can be traced up to the neck or rather up to the level of the ear in the middle line where it appears to end in a blind diverticulum.

Limbs: - The upper and lower limb bones are well formed and are fully representative except the carpals wherein no bones are visible and the tarsals wherein only two bones are seen on each side. The pelvic bones are well formed.

Dissection

Opened from the front in the middle line, the thorax and abdomen were seen to be differentiated by a well-formed diaphragm. The thoracic cavity is single, and divided into three portions by the mediastinum. Lungs: fair-sized, one on each side. Heart: single, well-formed, enclosed in the pericardial sac. Aorta: single and at once gives off a thick branch (innominate artery) which again divides into two branches, one for each side of the head of the right baby, while a third posterior branch supplies the right upper extremity. Then the aorta gives off two branches, one for each side of the head of the second foetus, while a posterior branch goes to the left upper extremity (figure 8).

In front of the heart, aorta, and its branches, is a very big lobulated thymus as a collar round the neck of both the foetuses. The peritoneal cavity is single, upper part of which is

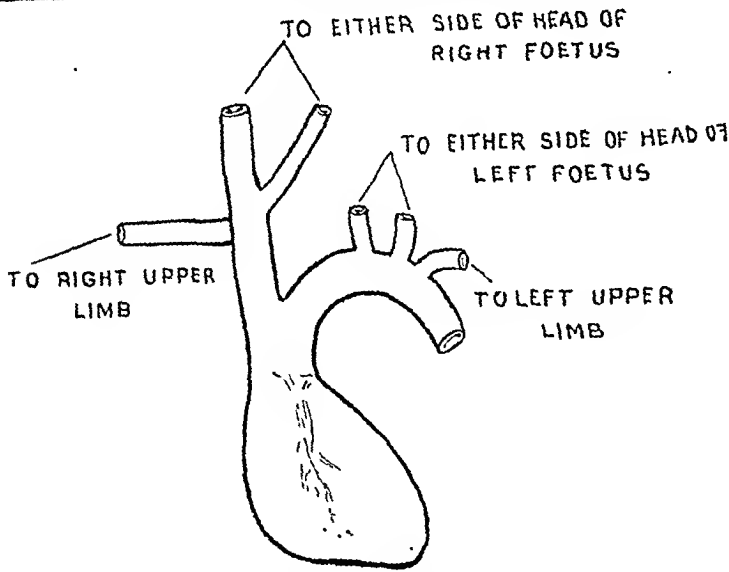


Fig. 8.—(Case 3.) Showing the branching of the aortic arch to supply the two heads and upper extremities.

occupied by a very big liver. Spleen is single, of average size and found at the left upper corner. Alimentary canal is single. Meckel's diverticulum is present. Appendix is rather big in size. Anal canal is formed and opens into the anal aperture at the normal site. Kidneys are two in number, right and left, from which two ureters drain into the urinary bladder. Penis is well formed and contains the urethral canal inside. Cranial cavity is empty. Eyes: two in each foetus, fairly well developed, from which rudimentary optic nerves come out and cross forming optic chiasma after which they are found to disappear as fibrous bands attached between grooves in the bones of the floor of the cranium. Spinal canal is empty. Spinal nerves are normally developed.

CASE 4 (CEPHALOTHORACOPAGUS JANICEPS)

Clinical notes: No history of the case is available.

Description (figures 9 and 10, plates XXVIII and XXIX)

The bodies of two well-developed twin babies (female) are separate and distinct below the level of umbilical region, while above this level they are joined front-to-front in the thorax, neck and head regions. The two heads have, as it were, been fused face to face into one. Viewed from one side, a pair of auricles is seen directed more in front, while there is a prominent chin, above which there is the rudimentary opening of the mouth, no trace of the nose is visible, while further up is one triangular opening representing the rudimentary eye. Viewed from the opposite side, the appearance is similar, excepting that the mouth opening is just a pin-hole.

Bones of the cranium are not developed properly. There are two pairs of upper limbs

and two pairs of lower limbs. General development is good. One umbilical cord is common to both.

Skiagram (figure 11, plate XXIX)

Each body has a separate vertebral column from the beginning to the end, and the appendicular skeletons are free and well developed. There is complete fusion of the cranial bones, wherein no separate bones are identifiable. The cranium is pear-shaped.

Dissection

Opened from one side, a well-developed diaphragm is seen separating the thoracic and abdominal cavities.

Thoracic cavity: Heart is single, situated centrally in the chest, very small in size. Lungs are rudimentary, one on either

side of middle line, in well-developed pleural cavities.

Abdominal cavity: There is a centrally placed, well-developed liver. There are coils of intestine which opens in the normal position into the anus. Spleen, kidneys, bladder are fully developed, and are in their normal sites. Uterus and appendages are in their normal position, but are rudimentary.

Opened from the opposite side, the appearances are similar except that the thoracic cavity contains a very small single centrally situated heart but no lungs.

The cranial cavity is empty, covered by a very thin membrane and scalp. Brain is not developed. The vertebral canals are empty. Spinal cords are not developed.

CASE 5 (PARASITIC MONSTER)

Clinical notes: No history of the case is available.

Description

A case of fused twins in which to the buttock of a fully developed foetus is attached the hind part of another foetus, rest of which is wanting.

First foetus: The head, upper and lower limbs are well formed. The trunk, excepting a deficiency at the lower part of the anterior abdominal wall (ectopia vesicæ), is also well formed. The genitals are represented by the stump of a penis with no urethra passing through it. To the perineum is attached the second foetus. Hence the anal aperture is absent in the normal position but opens in a cloacal aperture (into which the urethra also opens) anteriorly at the left inguinal region.

Second foetus: The head, trunk and upper limbs are absent. The buttock fused anteriorly to the perineum of the first foetus. The left

leg is fully developed and crosses over the right thigh of the first foetus. The right leg is represented by a pear-shaped mass, 4 inches by 3 inches, from the free end of which projects what appears to be a fully developed toe with a fully developed nail.

Skiaogram (figure 12, plate XXX)

First foetus : The pelvis is broadened and opened out, so that the legs pass outwards. The sacrum is bent to the right.

Second foetus : Fused to the pelvis of the first foetus are the apparent rudiments of the pelvis of the second foetus, from the side of which arises its well-developed left leg, while the other pyriform lump shows a long bone. The rest of the skeleton of the second foetus is not seen.

Dissection

First foetus : Heart, lungs, kidneys and other organs are normally developed and are in their normal positions. The rectum passes from the right side of the peritoneal cavity to the left, dips down behind a horn-shaped process (composed of cartilage) and opens in front in the left inguinal region in a cloacal aperture, through which meconium is seen to come out. The urinary bladder is rudimentary and is not in proper position. It is at the base of the pyriform mass just adjoining the cloacal aperture wherein it also drains.

The pyriform mass on being opened was found to be composed of subcutaneous adipose tissue. Two thin, long, cartilaginous bones were found in it.

Discussion

The last three cases are examples of malformations involving more than one individual (duplicate monsters). Duplicate monsters are twin foetuses developed from a single ovum, and organically united by some parts of their bodies. Duplicate monstrosity is a rare condition, frequency being stated as one in fifty thousand births. They are extremely rare, and of much interest to the anatomist and the pathologist, as well as to the gynaecologist, for they sometimes feature in cases of obstructed labour (if the foetuses are of average size, usually they are small and spontaneous delivery may sometimes occur).

Before we enter into the discussion of the last three malformations reported above, it has been thought advisable to give a short résumé of the various anomalous conditions affecting more than one individual, for the convenience of the reader. The following scheme is adapted from Marchand :

1. Both bodies derived from anlagen which developed from one ovum and which were originally similar and symmetrical : symmetrical duplicity :

(A) Both bodies originally complete : complete duplicity :

(i) The two bodies remain separate; union confirmed to chorion; twins.

(ii) The two bodies united : formed alike (equal) or one remains more or less rudimentary (unequal) : duplicate monsters (asymmetrical disomata).

(a) Union confined to lower end of body; double monsters with posterior union; anterior duplicity (terata anadidyma).

(b) Union confined to middle of body, or extending from middle forward; double monsters with middle union; anterior and posterior duplicity (terata kata-anadidyma).

(c) Union confined to upper end of body, or extending from upper end downward; double monsters with anterior union; posterior duplicity (terata katadidyma).

(B) Duplicity does not affect entire anlage but only a part : incomplete duplicity.

(i) Two incomplete anlagen pass over into a single anlage; posterior incomplete duplicity.

(ii) An originally single anlage forms by dichotomous growth two separate upper (anterior) ends; anterior incomplete duplicity; in addition, triplicity, quadruplicity, etc.

2. Two bodies derived from two originally dissimilar, asymmetrical anlagen, of which one, always rudimentary, becomes more or less enclosed and nourished by the other; true parasitic duplicity; asymmetrical duplicity; (asymmetrical disomata); in addition, teratoid tumours.

The third case reported above is an example of monster with superior incomplete duplicity (diprosopus tetrophthalmus), with anencephaly and craniorachischis. The development of the brain and of the spinal cord have been arrested at the stage reached at about the fourth week, when the neural plates should have closed behind to form the brain, but which are still apart, and the mesodermal tissue which would have developed into the cranial cavity and the membranes, are still unchanged; thus the neural plates lay exposed to the amniotic fluid at the cephalic extremity and hence they atrophied. The presence of cicatricial tissue in this part indicates that circulatory failure was the cause of anencephaly.

Case 4 is an example of monster with anterior union, the type of union being ventral (cephalothoracopagus janiceps). This monster has four upper limbs, which is rather uncommon, for all such monsters usually have one set of upper limbs.

Case 5 is an example of asymmetrical disomata (parasitic monster) with some rotation, bringing the left leg of the parasitic foetus over the right of the autosite. The second foetus is attached as a parasite to the first foetus, depending upon

it for its nutrition, and has developed at least one complete part, viz. the left lower extremity, together with a rudimentary pelvis and a rudimentary right lower extremity.

Two groups of factors mainly concerned in the production of a monster race: (1) Germinal or hereditary factor. Certain malformations, even so great as to put the foetus in the class of monsters, have been known to occur in families through successive generations. Probably there is something more in it than mere coincidence.

(2) External influences acting on a normal germ. Experimental work has decisively shown that monsters can be produced in lower animals by subjecting the living egg or young embryo to unusual conditions, mechanical or physico-chemical. So many malformed human embryos resemble in a general way and often in detail the monsters in the lower forms of animals produced by experimental means, that a probable similarity in the causation of them at once suggests itself.

According to Mall (1908) the primary disturbing factors in human beings are not poisons in the maternal blood, corresponding with chemical agents used in experiments, but the faulty implantation of the ovum in the uterine mucosa, resulting in disturbance of its nutrition and consequent faulty development. The most plausible explanation of faulty implantation is that some form of endometritis makes the uterine mucosa incapable of adapting itself for the reception of the ovum.

Stockard, on the basis of extensive experiments on animals, was led to the conclusion that changes in the conditions of temperature and oxygen supply are the most frequent causes of abnormal and monstrous development. In mammals, with their relatively constant temperature, the developmental environment is under natural control, but if there is lack of perfect regulation, there may be disturbances in oxygen supply which are regarded as potent factors in the production of monsters. Shock, worry, deprivation, etc., on the part of the mother may produce vascular and nutritional disturbances in the endometrium which may seriously affect the growth of the ovum (DeLee, 1938; Ballantyne, 1904).

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SEPARATION OF LIDS BY LID SUTURES IN CATARACT EXTRACTION

REPORT ON FIFTY CASES

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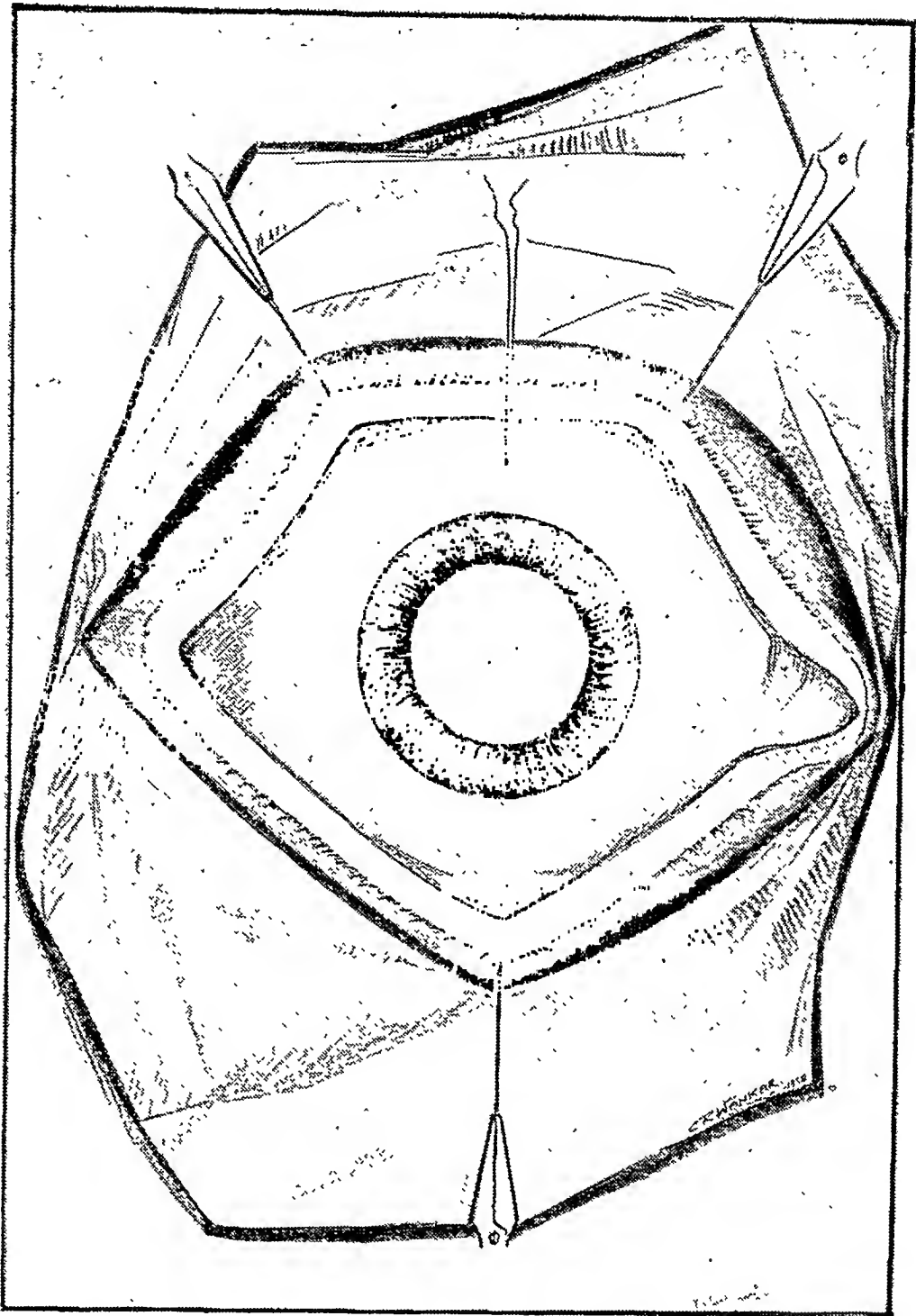
At the time of cataract extraction, the separation of lids and their maintenance in that position during the whole of the operative procedure have always been a headache for the ophthalmic surgeon. The traditional eye speculum, which has been used so far by nearly all the eye surgeons in this country, has the disadvantage that, in addition to retraction of the lids, its blades cause pressure on the globe and thus can easily be one of the factors in the causation of the escape of vitreous, even if the akinesis be thorough. To avoid this, the lid sutures have proved to be of great value. The procedure of their insertion is simple and is described below:

Washing of the conjunctival sac, surface anaesthesia and akinesis, etc., have already been done and patient is on the operating table. 0.2 cc. of 2 per cent novocaine is injected subcutaneously at three points, two on the upper and one on the lower lids. The points on the upper lid are at the junction of the lateral one-third with the medial two-thirds, and the other at the junction of the medial one-third with the lateral two-thirds, both these points being 2 mm. from the lid border and on the skin side of the lid. The point on the lower lid is in the centre and placed similarly 2 mm. from the lid border.

Sterilized towel with an opening for the affected eye is placed on the head and face. Horse hair mounted on fully curved needle is passed through the three points injected already. Each horse hair is pulled gently so as to retract the lid and is attached to the towel by small artery forceps as illustrated.

Advantages

1. Full retraction of the lids is caused and maintained without the help of the assistant.
2. No pressure is put on the eye-ball and therefore the danger of escape of vitreous is minimized.
3. Material used is simple and there is no difficulty of its procurement.



Disadvantages

1. Two to three minutes more are required.
2. There are three additional pricks for the patients to bear.
3. Greater traction may cause tear of the skin by the sutures.
4. Hæmatomata may form on the lids at the site of the sutures.

(Disadvantages nos. 3 and 4 appear to be only theoretical, as the author did not come across them in any patient in his series.)

5. Upper lid may be partially everted. This only occurs if the distance of the suture from the lid border is more than 3 mm. Fifty cataract patients were selected for the application of lid sutures in this series in six months from 1st

July, 1949. Vitreous escape did not occur in any patient. Forty-two were extra-capsular and 8 intra-capsular extractions.

N.B.—The central upper suture in the illustration is Superior Rectus stitch.

TREATMENT OF INFANTILE CIRRHOSIS OF THE LIVER

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Introduction

Sixty years ago, Sen (1890) published an article on the 'Cirrhosis of the liver in children'

in the *Indian Medical Gazette* and therein he remarked that 'the aetiology of this fatal disease, more certain of its victims than even of the dreaded cholera or smallpox', is in darkness.

In 1880, the *Indian Medical Gazette* wrote in a leading article on 'Hepatic cirrhosis in children' as follows: 'Is the disease which has attracted attention in Calcutta really cirrhosis? If so, what is its cause? Syphilis, struma, malaria, faulty hygienic or dietetic error, or some other undiscovered and unsuspected factor? Does the disease occur elsewhere in Bengal or India? We trust that the observation will have the effect of attracting to it many workers or eliciting much light on what must be confessed as still an obscure subject'.

Several workers in India have from time to time attempted to explain the causative factors and the treatment of the disease. It would not be out of place to draw attention to a few of them because it is within the knowledge of every medical man that a thorough knowledge of the pathology and causal factors are the guiding principles for a rational line of treatment of any disease. Gibbons (1887), after a study of the post-mortem examination of the liver on four cases, described the condition as that of biliary cirrhosis. Green-Armytage (1926) attributed the pathological condition of the liver to the general deficient nature of food and the lack of essential salts and endoerines in cow's milk on which the children were fed. Radhakrishna Rao (1935) in an exhaustive description of the histopathology of the liver designated the morbid condition of the liver as one of 'sub-acute toxic cirrhosis'. In 1941, I published a paper on the aetiology and pathology of this disease after a study extending over a period of 10 years. I have shown therein that the pathological change brought about in the liver is that of 'Portal or Laennec' type of cirrhosis, the causative factors being cow's milk in the beginning and subsequent infection of the liver by *B. coli*. This article drew the attention of several workers in India and abroad.

The *Journal of the British Medical Association* (1943) in an editorial has traced in a concise manner the progress of knowledge in regard to the aetiology of cirrhosis of the liver from the time of Laennec (1819) up to Rao (1941, the author of this paper). I consider it necessary to reproduce a few important points mentioned in that article as an introduction to the subject of treatment of infantile cirrhosis of the liver.

'The term cirrhosis was introduced by Laennec for a condition which in many ways presents as enigmatic a problem as any other in medicine. There has consequently been no shortage of descriptive terms and attempt at classification; atrophic and hypertrophic cirrhosis, portal, biliary and Hanot's cirrhosis, mono- and multi-lobular cirrhosis and hobnail or

gin-drinker's liver have all had their vogue. Out of a chaos an orderly system is now perhaps emerging which will mean something to the clinician. The tendency now is to recognize two main types namely portal and biliary (obstructive and infective). But we still seem to be far from a complete understanding of the aetiology and pathogenesis of cirrhosis. The cells of the liver are bathed in blood brought by portal circulation and so are exposed to any noxious agent that travels along this well-worn route. According to the nature and extent of the injury a few may die; reaction may be severe or mild, . . . and insidious; whatever the beginning, the end may be cirrhosis. György and Goldblatt (1942) found that in hepatic injury of dietetic origin (necrosis and cirrhosis with or without ascites) determining factors seem to be connected with the lipotrophic action of casein. Previous experiments showed that focal or diffuse necrosis was observed in rats fed on a diet devoid of vitamin B complex. They believe that the lipotrophic action of casein is in direct proportion to its contents of methionine and to the presence of choline in the diet, and that it is reversely influenced by l-cystine and supplements of fat. Some corroboration of reported beneficial effect on cirrhosis in man of a highly nutritious diet supplemented with the vitamin B complex comes from Patek and Post and from Lowry *et al.* (1941) of the beneficial effect of choline, high casein diet, or choline with a high casein diet in rats with hepatic cirrhosis produced by low casein and low choline diet with added cystine. Patek and Post (1941) suggest that there is an aetiological relationship either direct or indirect between nutritional deficiency and cirrhosis of the liver. Lack of essential factors might lead directly to the development of the disease, while the malnourished liver becomes more vulnerable to toxins. Spellberg *et al.* produced cirrhosis of the liver in rabbits and fatty liver in guinea-pigs by feeding the animals on apparently adequate diets containing 20 per cent of fat, chiefly butter fat, although some factor other than diet might have been responsible. In view of these results, those of Rao suggesting that the infantile cirrhosis of Hindu children (a variety of portal cirrhosis) is caused by a diet of cow's milk combined with *B. coli* infection, must seriously be considered. There is scope of further work along these lines'.

Bicknell and Prescott (1946) have stated in their book on 'Vitamins in Medicine' that 'Lowry and his co-workers produced cirrhosis of the liver in rats resembling Laennec's cirrhosis in man. Choline both prevented and cured the condition although as would be expected the fibrous tissue persisted. Similar findings are reported by Fouts (1943). Milk is not a very good source of choline (1.07 mg. per gm.) and the suggestion of Rao that the infantile cirrhosis seen in Hindu children (a variety of portal

cirrrosis) may be caused by a diet of cow's milk and *B. coli* infection merits consideration. Recent clinical studies also point out the importance of a high protein diet in the treatment of patients with hepatic lesions*.

The pathological changes brought about in the liver of infantile cirrhosis also gives us an insight into the ætiological factor of the disease. Until recently, the morbid condition of the liver was considered to be that of biliary cirrhosis; but I have shown in my previous publication that the changes brought about are of 'portal' or 'Laennec' type of cirrhosis, due to inflammatory changes. I have also pointed out that the correct nomenclature of this disease should be 'Infantile cirrhosis' and not 'Infantile biliary cirrhosis'. (It is gratifying to note that in the recent publication of Manson's Tropical Diseases—Manson-Bahr, 1945—the name of the disease has been altered according to my suggestion.) So far as this disease is concerned, there are two factors which bring about the disease, viz, (1) cow's milk and (2) *B. coli* infection. Cow's milk evidently is lacking in certain essential food factors, especially choline, and renders the liver vulnerable to infection. *B. coli*, which is always present in the intestine, becomes pathogenic and produces a low grade of inflammation of the liver resulting in the formation of cirrhosis. The logical treatment therefore would be to tackle the two causative factors adequately and systematically.

Treatment

In the first series of cases, six children who had not developed either jaundice or ascites were selected for treatment.

Diet.—The first and foremost advice given to the mother was to stop feeding the child on cow's milk and to give one of the proprietary milk-foods* that was available in the market. Secondly, in order to increase the protein contents of the diet, protein hydrolysate (casein hydrolysate) was given 2 to 4 teaspoonfuls a day. Oranges and tomatoes were also given to make up the vitamin C factor. Small quantity of rice was allowed to be given for such of these children who were above 2 years of age. No restriction was placed on the use of sugar and common salt in the diet.

Medicinal treatment.—Choline was administered in the form of a mixture, 15 to 20 grains per dose, three times a day.

Hepatic mixture (containing acid hydrochlor. dil., tinct. nux vomica, ammonium chloride and tinct. gent. co.) was given in drachm doses twice a day, each time about half an hour after food. Constipation was corrected by giving Hydrarg. cum cretæ or milk of magnesia, whenever necessary.

*The proprietary milk-foods usually available here were Glaxo, Cow & Gate, Ostermilk, Similac and Nestle's food.

Injections.—Vitamin B₁₂ complex containing 10 gm. of thiamine chloride per dose was injected once in 2 days hypodermically. Auto-vaccine of *B. coli*, prepared from the cultures of stools of these children, was given in divided and gradually increasing doses on alternate days beginning from 0.1 cc. up to 1 cc. per dose from an emulsion containing 1,000 million organisms per cc. Later on the 1 cc. dose was maintained for nearly 2 months, the injections being given at weekly intervals. The total period of treatment was from three to four months for each child. There was complete recovery in four cases from out of the six that were chosen for treatment. In the case of the other two children, the parents were not able to attend the hospital regularly and as such those children developed ascites and died.

Streptomycin.—While I was about to report on the success of the above line of treatment, information was received (in the early part of 1948) that streptomycin was released for distribution to the hospitals under proper control by the Government of India. As it was reported in the literature that streptomycin acted on most of the gram-negative organisms including *B. coli*, I naturally felt that this drug should be of great benefit to the children suffering from cirrhosis of the liver. Accordingly, I selected three cases and treated them in the manner detailed below:—

Case 1.—Male child, 2 years of age, liver enlarged $3\frac{1}{2}$ fingers on the right and $1\frac{1}{2}$ fingers on the left side, no jaundice or ascites. Half a gramme of streptomycin hydrochloride (Squibb) was injected intramuscularly in two doses of $\frac{1}{2}$ gm. each, once in the morning and again in the evening for four days. As there were no signs of untoward reaction due to the drug, a single dose of half a gramme per day was adopted for the next 8 days until 6 gm. were finished in all. After an interval of 7 days by which time the liver was reduced to one finger-breadth, another course of 5 gm. was given in 10 days. By this time the liver was reduced almost to its normal size without any kind of complication. Injections were stopped and oral administration of vitamin B complex was continued for a period of three months. It is nearly two years now since the commencement of treatment, and the child is perfectly healthy.

Case 2.—Male child, one year old, liver enlarged $1\frac{1}{2}$ fingers. Streptomycin injections were given in $\frac{1}{2}$ gm. doses daily for 8 days. On the 12th day, the liver was found to be reduced to its normal size. Oral administration of vitamin B complex was continued for a period of three months. The child is perfectly healthy now.

Case 3.—Female child, $1\frac{1}{2}$ years old, liver enlarged $2\frac{1}{2}$ fingers on the right side and one finger on the left. No jaundice or ascites. Streptomycin injections of $\frac{1}{2}$ gm. per day were

given and at the end of 10 days the liver was reduced to one finger-breadth. A total quantity of 9 gm. of streptomycin was given spread over a period of 25 days. The liver came to the normal size by this time. The child is healthy now.

In these three cases *B. coli* vaccine was not administered. All possible laboratory tests were done to make sure that they were genuine cases of infantile cirrhosis. All these children were fed on cow's milk since their birth before they became ill.

Simultaneously, I treated 2 more cases of advanced cirrhosis with ascites and jaundice. Streptomycin was found to be of no use in these cases.

For the last one year injections of streptomycin with oral administration of vitamin B complex and choline have become the routine treatment in this institution. Several private medical practitioners, that referred their cases to me, have also been treating them at their houses, on the lines mentioned above. It is gratifying to report that the results are very good.

Discussion

I am aware that the number of cases treated so far is small, but yet considering the fact that it is not an easy matter to get a large number of children at any one time for treatment, partly due to the natural apathy of mothers to subject their children for repeated injections and to a large extent due to the inconvenience and the cost involved in bringing the children to the hospital for months together, there is sufficient justification in publishing the results of treatment of these few cases.

One can say now with confidence that we are no longer in 'darkness' regarding the aetiology and the methods of treatment of this dreaded disease. I am sure, streptomycin will prove almost a 'specific' for infantile cirrhosis aided by choline and other vitamin B factors. I am also sanguine that this disease could be prevented if those children (particularly of the vegetarian family) that do not get sufficient quantity of mother's milk should be fed on a proprietary milk-food instead of cow's milk. Vitamin B complex and milk-foods are easily available in the market and the latter are even cheaper than the so-called cow's milk sold in the cities nowadays. If the mothers do want to give good cow's milk, they may do so just only once or twice for the whole day (so as to form a small part of the diet) provided they give proprietary milk-food to form the major part of the diet. It is incumbent on such mothers who have lost the previous child or children on account of cirrhosis to avoid feeding the children born subsequently with cow's milk. They should also consume fairly good quantity of vitamin B complex, during pregnancy, to prevent development of cirrhosis in the children to be born.

Summary

1. Recent knowledge about the causative factors of cirrhosis is malnutrition, especially the lack of proteins in adequate quantity and vitamin B complex in the diet is reviewed. The lack renders the liver vulnerable to 'toxins' which produce cirrhosis. In the case of infantile cirrhosis, cow's milk, being deficient in certain essential food factors and choline, devitalizes the liver and later on *B. coli* infects the liver and produces cirrhosis.

2. Choline is considered to be capable of preventing the formation of cirrhosis when it is present adequately in the diet and also of curing the condition when cirrhosis has developed.

3. The treatment I adopted in the beginning was to administer choline orally and to give injections of *B. coli* vaccine in gradually increasing doses. But later on the injections of vaccine were given up and streptomycin was used in its place.

4. Streptomycin, choline and vitamin B complex appear to be almost 'specific' in curing infantile cirrhosis.

5. Infantile cirrhosis could be prevented if children that cannot get mother's milk altogether, or when the quantity is not sufficient, are fed on proprietary milk-foods instead of cow's milk and also given vitamin B complex orally.

Great difficulty was felt to obtain choline to treat the cases of infantile cirrhosis and I acknowledge with grateful thanks the help rendered by The British Drug Houses Ltd., in sending me a large quantity of choline chloride (free of cost) in response to my general request to most of the well-known firms to send me the drug to carry out investigations in the treatment of this disease. I convey my thanks to the medical officers of the Victoria Hospital for supplying me with streptomycin whenever required and also giving me all other possible facilities to carry on this special work. I am also grateful to all the private medical practitioners who referred their cases of infantile cirrhosis to me and also co-operated with me in treating those children on the lines suggested by me.

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CHLOROMYCETIN IN TYPHOID AND PARATYPHOID FEVER

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THE first reports on the action of chloromycetin on typhoid were published about two years ago (Woodward *et al.*, 1948), but it is only since last year that this new antibiotic has become available in India. A fair number of reports have appeared since in the literature in India and abroad which show that chloromycetin has a specific action in typhoid fever.

Typhoid fevers, apart from occasional outbreaks, have become a rarity in Western countries. In India, typhoid is still a very common disease, and, though its treatment underwent a profound change during the years before the war, when it was believed that typhoid cases had to be starved, even with improved nursing and a diet containing liberal amounts of calories and vitamins, it still carried a high mortality. Every typhoid case presented a serious problem and there was never any certainty as to what the next day might bring until the temperature had remained normal for a fairly long period.

Since the middle of 1949, when chloromycetin first became available here, seven cases have come under my observation, who were successfully treated. Three of them were cases of paratyphoid. Two of those paratyphoid cases were severe, and are particularly worth recording as they came under treatment within the first few days of the disease. All cases, except one, were treated within the first week of the disease.

The first opportunity to use chloromycetin came on 8th July, 1949, when I saw a European male, aged 29 years, who had become ill with fever and headache on 3rd July, but had still attended office on 4th July. On 8th July his highest temperature was 103.6°F., on 10th July it rose to 104°F. and he showed a few typical rose-spots. There also was some enlargement of the spleen. There were no severe constitutional symptoms. The agglutination test was confusing, the Widal being positive: 1/50 for para A and 1/25 *Sal. typhi* and negative for para B and C.

Blood culture was negative. Chloromycetin treatment was started on 11th July. Only three bottles were available at the time. One bottle was taken as the first dose, followed by one capsule 2-hourly. Within two days the temperature had become normal, but the chloromycetin was exhausted. On 17th July, the temperature rose again above 99. Only one bottle of chloromycetin was obtainable which was given 4-hourly. Within two days the temperature had settled down to normal again and remained normal.

Stool examination on 16th August, one month after defervescence, still showed typical colonies

of *Sal. typhi*. Two weeks later stool examination had become negative. Urine culture was twice negative for *Sal. typhi*.

A typical example of abortive treatment of typhoid is the following one: A European girl, aged 18 years, seen first on 1st January, 1950. For the last three or four days she had not felt quite well, but had not taken any notice of it. On 31st December, 1949, she had gone to a party from which she was forced to return home as her temperature rose to over 103°F. On 1st January at 1 p.m., her temperature was 103°F. but there were no severe constitutional symptoms. The Widal test taken on 2nd January was positive for *Sal. typhi* 1/125. Chloromycetin was started on the evening of 2nd January: on 5th January the temperature was normal and remained normal. Culture of blood and stool and urine remained negative (chart 1).

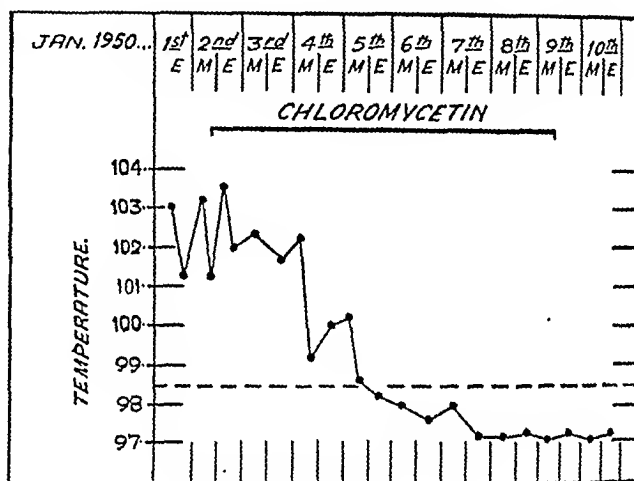


Chart 1.

The following case must be considered a severe infection complicated by malaria:

The patient, European male, aged 30 years, fell ill with slight fever, 99.4°F. on the evening of 29th December, 1949, outside Calcutta. During the following days his temperature was always high, around 103°F., not below 100°F. On 30th and 31st December he was repeatedly sick, vomiting bile with fair amounts of blood. A tentative diagnosis of malaria was made, but given up when no plasmodia were seen, and no specific treatment was given until 8th January when the patient whose condition was deteriorating very fast was brought by plane to Calcutta. When I saw him first, on 8th January, 1950, rather late in the evening, he was extremely toxæmic. It was very difficult to obtain a history from him because of his drowsiness. His pulse was rather weak and dicrotic, his abdomen was tympanitic and his spleen was very large, 4 inches below the costal margin and very tender. There were no rose-spots. The patient appeared to be so critically ill and the diagnosis of typhoid so obvious that chloromycetin was started at once, without waiting for the result of blood examinations which could not have been performed until the following day. However,

I took a blood slide in order to see whether the blood count was in accordance with the diagnosis of typhoid. To my great surprise I saw a fairly heavy infection with B.T. On 10th January, the Widal test was positive 1/125 for *Sal. typhi*. The clinical course is shown in chart 2. Treatment for malaria was instituted on 9th January with quinine orally. The rise of temperature on 10th January is more likely to have been caused by malaria than by typhoid. Plasmodia were not seen any more on 12th January. Chloromycetin dosage: first dose 3 g., followed 2-hourly by one capsule 0.25 g., in all 6 g. It is of interest to note that chloromycetin was tolerated extremely well even in the combination with quinine and there was not any accentuation of toxic symptoms as described in the literature.

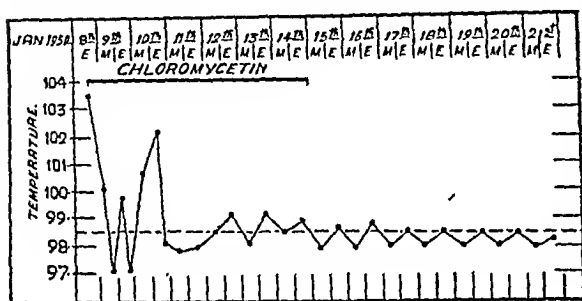


Chart 2.

Of the three paratyphoid cases treated with chloromycetin, one, a European male, aged 38 years, was of very mild nature. His temperature was only 100.4°F., highest at the beginning of the treatment, and chloromycetin brought the temperature to normal after 48 hours. Blood culture was negative, the Widal test for paratyphoid B was positive 1/250, negative for *Sal. typhi* and para A.

In the following case, however, the effect of chloromycetin was dramatic. This patient, a European male, aged 36 years, consulted me on 19th November, 1949, with the history of slight rise of temperature for four days, up to 100°F. in the evening and stated that the disease had started with some diarrhoea. He had been working until the day before and his temperature had been normal every morning. On examination nothing of importance was found. His blood was taken for Widal tests and for malaria and he was advised to stay in bed. That same afternoon his temperature rose to 102.2°F., he looked and felt now quite ill and was transferred to a nursing home. Late in the evening the blood examination was reported: positive 1/125 for paratyphoid B, negative for paratyphoid A and *Sal. typhi*. During the night the patient became extremely ill. He was shivering and perspiring alternatively and next morning he was very toxæmic, unable to speak coherently, unable to empty his bladder and the clinical picture of this sudden, severe prostration

resembled much more that of a cerebral malaria than of typhoid. Chloromycetin treatment was instituted, 3 g. first dose, followed by 0.25 g. 2-hourly. Repeated examinations for malaria plasmodia remained negative, though again on the following day the clinical impression was far more that of cerebral malaria than of paratyphoid. The patient remained confused and almost unable to speak. During the following night, however, there was a sudden improvement, the temperature fell to normal and remained there (chart 3).

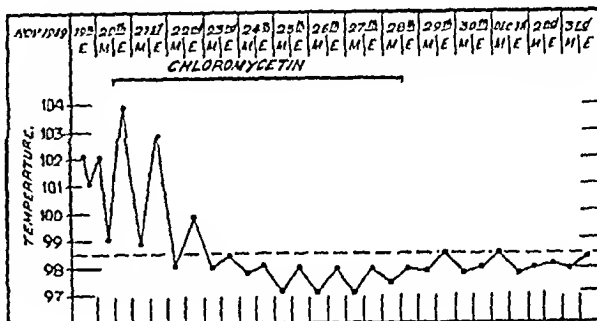


Chart 3.

Although there had been only two and a half days of fever, this short attack had been accompanied by such severe toxæmia that the patient was not able to stand when he was allowed to get up for the first time after his temperature had remained normal for ten days. If chloromycetin had not been available in this case, the prognosis would have been very grave. The severity of the condition had become manifest before chloromycetin treatment was started. Within 48 hours this severe paratyphoid infection had been brought under control without producing any unpleasant by-effects. Culture examination of stool, blood and urine remained negative.

Total dose of chloromycetin was 21 g.

The next case, European male, aged 20½ years, probably derived his infection from the same source as the previous case. Though he acquired his infection in another house, both patients obtained their food from the same kitchen.

When seen first on 19th December, 1949, he reported that his disease had begun five days before with diarrhoea, lasting for two days. Since then he had had slight fever in the evening and normal temperature in the morning. On 19th December his temperature rose to 102°F. (*vide* chart 4, axillary temperature). Next day the fever remained unchanged but blood examination for malaria was negative. On 21st December Widal was found positive 1/125 for *Sal. typhi* and para B. Chloromycetin was started, 3 g. first dose, followed by one capsule 2-hourly. On the day chloromycetin was started, the patient looked severely ill for the first time, he was slightly drowsy and also showed a definite enlargement of the spleen. No rose-spots were

seen. On the 4th day after beginning of chloromycetin treatment, the temperature became normal and remained so. Blood culture showed *Sal. typhi* as well as *Sal. paratyphi B*. On 3rd January, 1950, eight days after defervescence, the stool culture still showed presence of *Sal. paratyphi B*. A fortnight later stool examination was negative for *Sal. paratyphi B*.

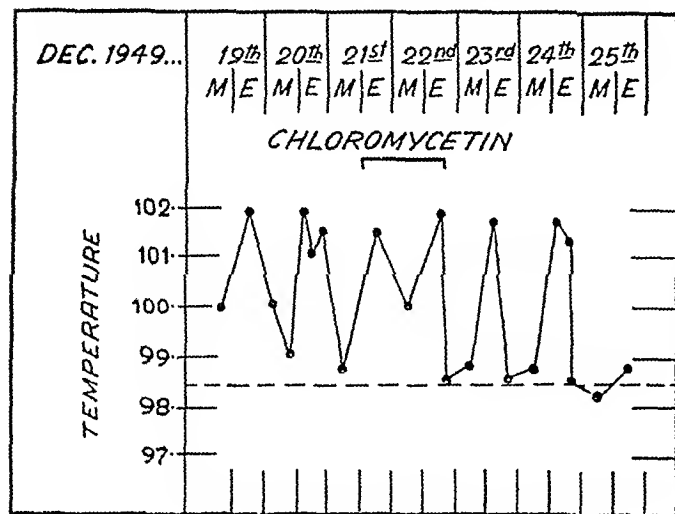


Chart 4.

In all 18 g. were given which were well tolerated and from the beginning of the chloromycetin treatment it was obvious that there was a steady subjective improvement though the temperature remained high for over three days.

One more case, comparatively mild of typhoid infection, was successfully treated with fall of temperature within 48 hours. The treatment was started on the 5th day of the disease. The Widal reaction was positive 1/125. The cultural examination of the blood was negative.

Discussion

In the present series of typhoid and paratyphoid cases, with the exception of one, treatment was begun at a very early stage of the disease. In all cases the Widal test was positive, though somewhat confusing in the first case, who, however, was exhibiting rose-spots, an enlarged spleen and who had a positive stool culture several weeks after defervescence. This case is of interest in another respect as chloromycetin could be given for three days only after which his temperature started to rise again. With one more phial of chloromycetin spread over two days the temperature was brought down.

There has been no relapse in the whole series. Patel, Banker and Modi's (1949) series of six typhoid cases, all with positive blood culture, came under treatment rather late, and they agree with Bradley (1949) that the full advantages of chloromycetin should be exploited best in cases whose treatment is begun within the first week. This desideratum is fulfilled in most cases of the present series and the dramatic effect of chloromycetin has been particularly striking in case 5 in whom treatment was begun on the 5th day of the disease, the second day of manifest illness.

This patient had been ambulant on the day before he became so severely ill that there was reason for the gravest anxiety if chloromycetin had not been available. The temptation to administer quinine as well was very strong, in spite of the negative findings for malaria because such sudden deterioration was thought to be not quite in keeping with the diagnosis of paratyphoid.

As far as I am aware, case 3 is the first described in whom malaria and typhoid have been treated simultaneously with quinine and chloromycetin. This combination did not appear in its effect to be more unpleasant than is expected from 30 g. of quinine per day. After three days of quinine treatment, while chloromycetin was continued, the patient was given paludrine, 0.6 g. per day, and recovery proceeded steadily. From another point of view also this case is of interest. For several months this patient had taken paludrine prophylactically, 0.3 g. per week. He had stopped taking paludrine a few weeks before the beginning of his present illness as he had thought that the malaria season was past. When he fell ill on 29th December, blood examination for malaria was negative. Obviously the typhoid had activated the malaria infection which had been suppressed by paludrine before.

Summary

Seven cases of typhoid and paratyphoid have been treated with chloromycetin, all, with the exception of one, having come under treatment within the first week.

In six cases the temperature returned to normal within 48 hours. In one case, in which paratyphoid B and *Sal. typhi* could be cultured from the blood, it took 72 hours for the temperature to become normal.

There has been no relapse in this series.

Chloromycetin had no unpleasant by-effects in any of these cases, not even when it was combined with full doses of quinine.

The effect of chloromycetin on *Salmonella* appears to be rather bacteriostatic than bactericidal as in two cases several weeks after conclusion of treatment *Salmonella* was still found in the stool.

My thanks are due to Dr. S. M. Ghosh of Central Calcutta Laboratories for his assistance in carrying out the serological and culture examinations.

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After conclusion of this paper the following remarkable case was observed:

The patient, a European woman, aged 40 years, had been inoculated against typhoid and paratyphoid in September 1949. On 19th February:

1950, she was feeling perfectly well and attended work in the morning as usual and a party in the afternoon. On 19th February morning she still felt well, but towards afternoon she was seized with a headache which became so unbearable that I was called to see her at 11 p.m. when her temperature was 102°F. Examination of the C.N.S. gave no clue to this extreme headache which had remained unchanged even after large doses of aspirin, and there was no rigidity of the neck.

Next morning at 7 a.m. the temperature had risen to 105°F. The patient was feeling very ill and drowsy. The examination of the C.N.S. as well as of chest and abdomen revealed nothing pathological. She was transferred to a nursing home. Blood examination on the morning of 20th February showed an essentially normal blood count, absence of malaria parasites, but a positive Widal reaction for *Sal. typhi* 1/125. At about 12 o'clock chloromycetin was started, 3 g. first dose; the evening temperature on 20th February came down to 102.4°F.; on 21st February the temperature fell steadily to 99.4°F. and reached normal on 22nd February, to remain there.

Reports of culture examination of blood and stool from two different laboratories were obtained on 23rd February, both positive for *Sal. typhi*.

There was no relapse.

Total dose of chloromycetin : 18 g.

In this case the very unusual features are the rise of temperature to 105°F. within the first 24 hours and beginning of chloromycetin treatment also within the first 24 hours. Proof of the diagnosis beyond doubt was obtained at a time when the temperature had already returned to normal.

The patient was so gravely ill that the impression was general that chloromycetin was life-saving in this case in which the disease began with extremely toxic manifestations.

A Mirror of Hospital Practice

ABSCESS BREAST

By A. G. CHACKO, B.A., M.B., B.S.
Quilon (Travancore)

I AM not sure whether I am writing anything new, but being encouraged with the excellent results obtained, I thought I would share my experience with others.

Abscess breast is a very common complaint down here in South India. The children are nursed not every three or four hours, but often every half an hour or oftener if necessary to stop the children from crying. The antenatal care of the nipples is unknown and no wonder the disease is so prevalent even among the educated. Added to this is the reluctance of the women-folk to reveal the nature of their complaint even to their own close relatives. The patients

come to us when they cannot bear the pain of the abscess any longer after spending many sleepless nights. The abscess by then is well formed and almost at the point of bursting.

The usual treatment with the majority of surgeons is incision, drainage and daily dressing, giving in conjunction with sulphadiazine or any of their favourite sulphanilamide preparations, or penicillin.

The difficulties of the rural medical practitioners are manifold. The patients have to come from a distance of even three to four miles. The transport difficulties and high fares, and the presence of other children at home with nobody to look after them, make it almost impossible for the women to attend the hospital regularly for dressings. Most of these abscesses even with the best care might take a pretty long time to heal, about two to three weeks or longer.

The routine treatment which I follow is aspiration of the abscess with a fairly thick, long aspirating needle and instillation of penicillin taking the usual aseptic precautions. Since I began aspiration for abscess breast, I have been very much surprised to find pus, more often than my previous estimate suggested. These abscesses are very thick-walled and it is very difficult to elicit fluctuation or other usual signs of an abscess. The amount of penicillin depends upon the size of the abscess cavity. About 2 or 3 lakh units of penicillin in aqueous solution can be injected in an abscess cavity of moderate size through the same needle which has been used for aspiration. The opening is sealed off with collodion or with tincture benzoin eo. Sulphathiazole in the usual doses by mouth or penicillin intramuscularly can be given if the patient can be hospitalized. These are not absolutely necessary. For patients living far off, I do nothing but aspiration and instillation of penicillin, to be repeated after two or three days.

Generally after two or three aspirations and instillations of penicillin, the abscesses heal up completely. Even at the time of the second aspiration, the aspirated material is much less viscous. As everybody knows, the response to treatment depends on the sensitivity of the bacterial organisms to penicillin and I am referring in this article only to those abscesses infected with the common pyogenic organisms.

Two case records may be interesting:—

Mrs. A., aged 25, pain and swelling of the right breast, 5 days' duration, temperature 101°F. Aspirated from the breast 2 ounces of thick pus and injected 2 lakh units of penicillin. Sulphathiazole 4 gr. a day also given. Patient came again on the 3rd day—no fever, pain much relieved. She does not want any more aspiration as she says she is cured. Aspirated again and a little clear fluid obtained—injecting another 2 lakh units of penicillin into the abscess cavity. Patient completely cured.

Mrs. P., extremely poor and living about 4 miles away, came with all signs of abscess left

breast. She cannot afford even to buy sulphathiazole tablets. Aspirated 3 ounces of very thick pus and injected through the aspirating needle 2 lakh units of penicillin. Patient came only after 4 days. She said she did not come as she was nearly all right. Aspirated again but only very little pus obtained. Injected another 2 lakh units of penicillin into abscess cavity. Patient completely cured.

Summary

A rapid and much less cumbersome method of treatment of abscess breast is suggested with aspiration of pus and instillation of penicillin.

AN UNUSUAL CASE OF ELEPHANTIASIS BUTTOCKS

By SUSIL KUMAR BHATTACHARJEA,
M.B. (Cal.), B.M.S.

Assistant Surgeon, Victoria Hospital, Darjeeling

THE common sites of elephantoid condition seen in the body are the lower extremities, external genitalia, anterior abdominal wall, breast and sometimes arms and face. The buttock as a site for elephantiasis one never comes across in any textbook of surgery and must be rare.

Case report

A Hindu widow, aged 45 years, was admitted into Khulna Sadar Hospital on 23rd November, 1945, with a huge swelling over both of her buttocks which, according to her, gradually increased within a course of three to four years. The cause of her seeking hospital help was that the swelling was not only very unsightly and an object of shame but it prevented her from walking erect and lying flat on her back. The patient gave a typical history of occasional attacks of fever (which has gradually become less and less in severity) along with pain and swelling over the buttocks, for a period of five to six years.

On admission, the patient was an obese woman near about the climacteric.

Both her buttocks were enormously swollen, rather hard and firm, the skin thickened, rough and warty in appearance, and showed some local dermatitis with intense itching which had developed very recently and prevented sleep at night (figure 1, plate XXX). She was running a low remittent temperature for several days past.

Her teeth and gums were bad and septic. Pharynx—normal. Bowel—constipated; no history of chronic diarrhoea or dysentery within the last three to four years.

Investigation

1. Blood—Hb. 60 per cent, red cells 2.8 million, white cells 11,500, polymorphs 78 per cent, eosino nil. Thick blood film taken at midnight showed *Microfilaria bancrofti* (although a bit unexpected).

2. Kahn's test—negative.

3. Stool—normal.

4. Urine—normal.

Treatment and progress

On admission of the patient, strict attention to the septic teeth, a course of sulphonamide drugs orally, followed by a course of arsenotyphoid injections were given. Locally, a ealamine-zinc-oxide lotion for the itching and dermatitis was used.

About a month and a half after admission, the patient was much improved. She was fever-free, the swelling slightly decreased in extent (specially over the left) and the local infective condition cleared. I next decided on an operation. Under general anaesthesia, elliptical wedges of thickened skin and subcutaneous tissues were excised from both the buttocks, keeping the shape and contour of the buttocks as far as possible, and the skin margins apposed and sutured with interrupted silk worm gut, leaving several tension stitches at the same time (figure 2, plate XXX). The convalescence was very satisfactory and union took place by first intention. The patient was discharged highly thankful twenty days after the operation and about two months after her admission into the hospital.

Discussion

The typical history of the case, the characteristic appearance and feeling of the local parts, the characteristic tissues removed at operation showing hypertrophy of both the skin and subcutaneous tissues and presence of microfilaria in blood set at rest all doubts regarding the diagnosis of the case. Microfilariae usually disappear from the blood when elephantiasis has set in apparently due to the obstruction of the lymphatic by the dead and disintegrated (often calcified) worm; but it is quite possible that the obstruction may be due to the presence of masses of living worms in a lymphatic or it may happen that some other lymphatic still lodges a living female worm which is parturizing hundreds of microfilaria without causing any obstruction or symptom.

The point of interest in this case is the unusual site. It is known that the particular type of infected mosquito bites a part of our body, the parasite enters through the puncture, finds out the nearest lymphatics, lodges inside a bigger channel and ultimately obstructs it, producing elephantiasis of the part drained by the lymphatic. If that is the pathology of the disease, then to my mind, the parts of the body most exposed to mosquito-bites and so carrying the chance of infection of the local lymphatics by the parasites are the parts usually affected. Mosquitoes usually bite us at night specially when we sleep, and as during sleeping-time we usually lie on our back, buttocks and back are relatively non-exposed parts to mosquito-bites and as such escape affection.

My thanks are due to the authorities of Khulna Sadar Hospital for their permission to use the case, note and the necessary data, and particularly to Dr. J. R. Banerjee, M.B., D.T.M., the then Civil Surgeon, Khulna, for his help and encouragement in reporting this article.

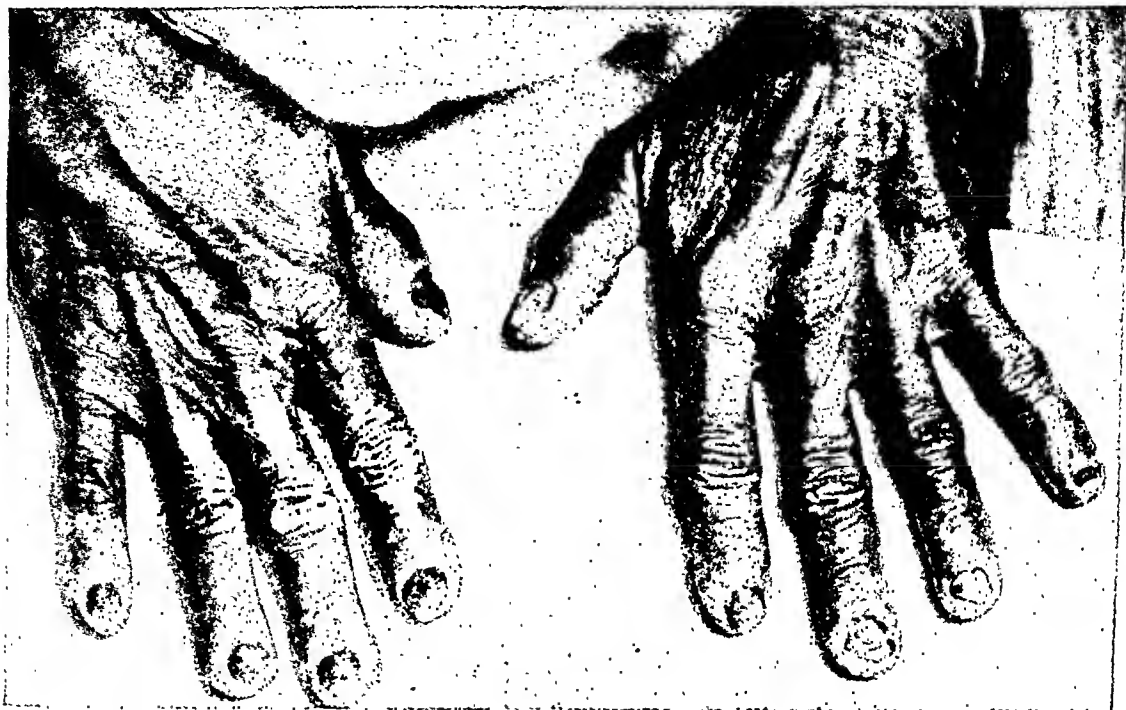
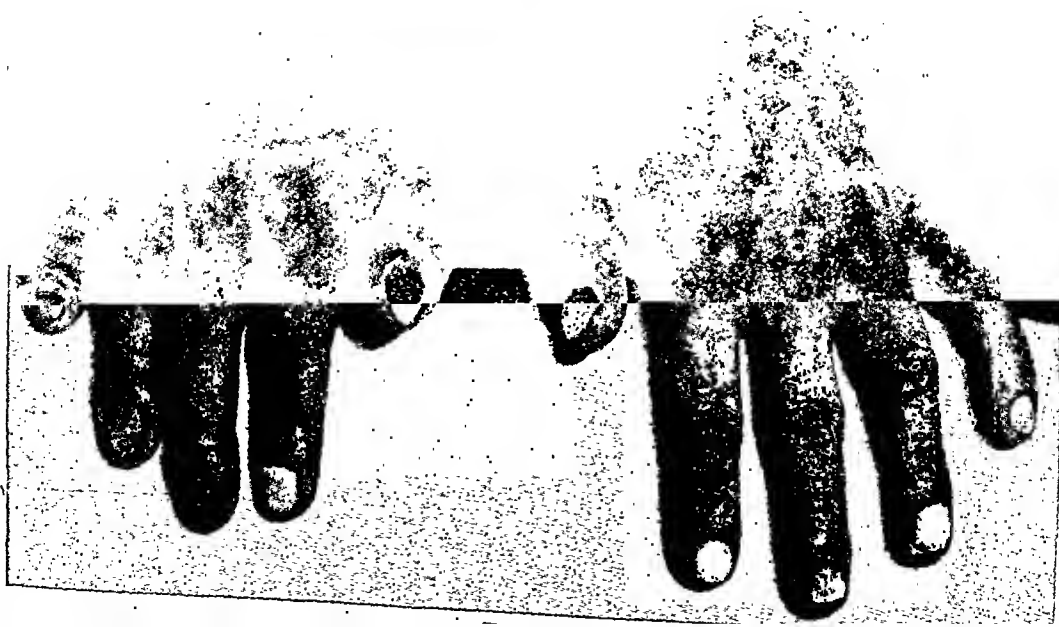


Fig. 1.



Fig. 2.



AN UNUSUAL CASE OF POST-KALA-AZAR DERMAL LEISHMANIASIS : P. C. SEN GUPTA, D. PANJA & A. K. BANERJEE. (O. A.)

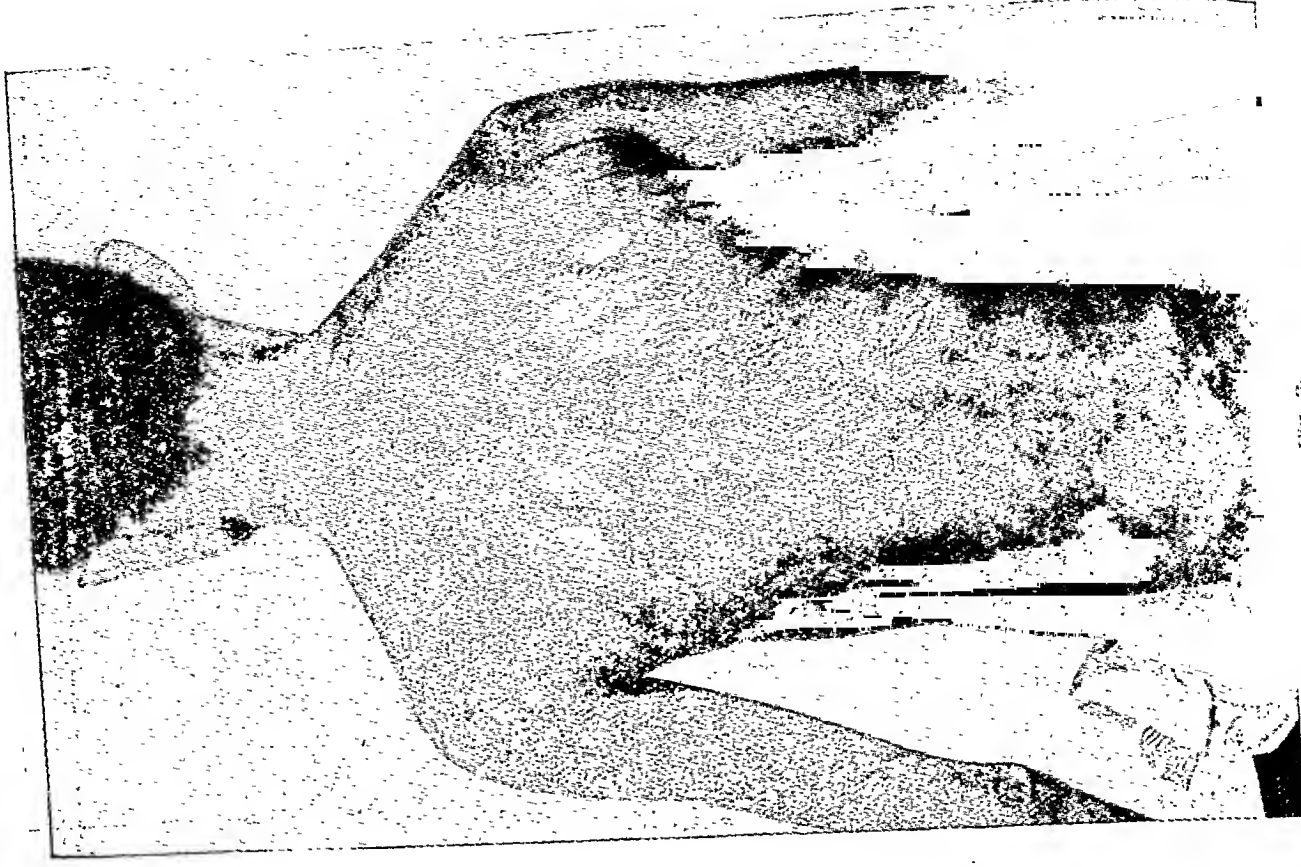
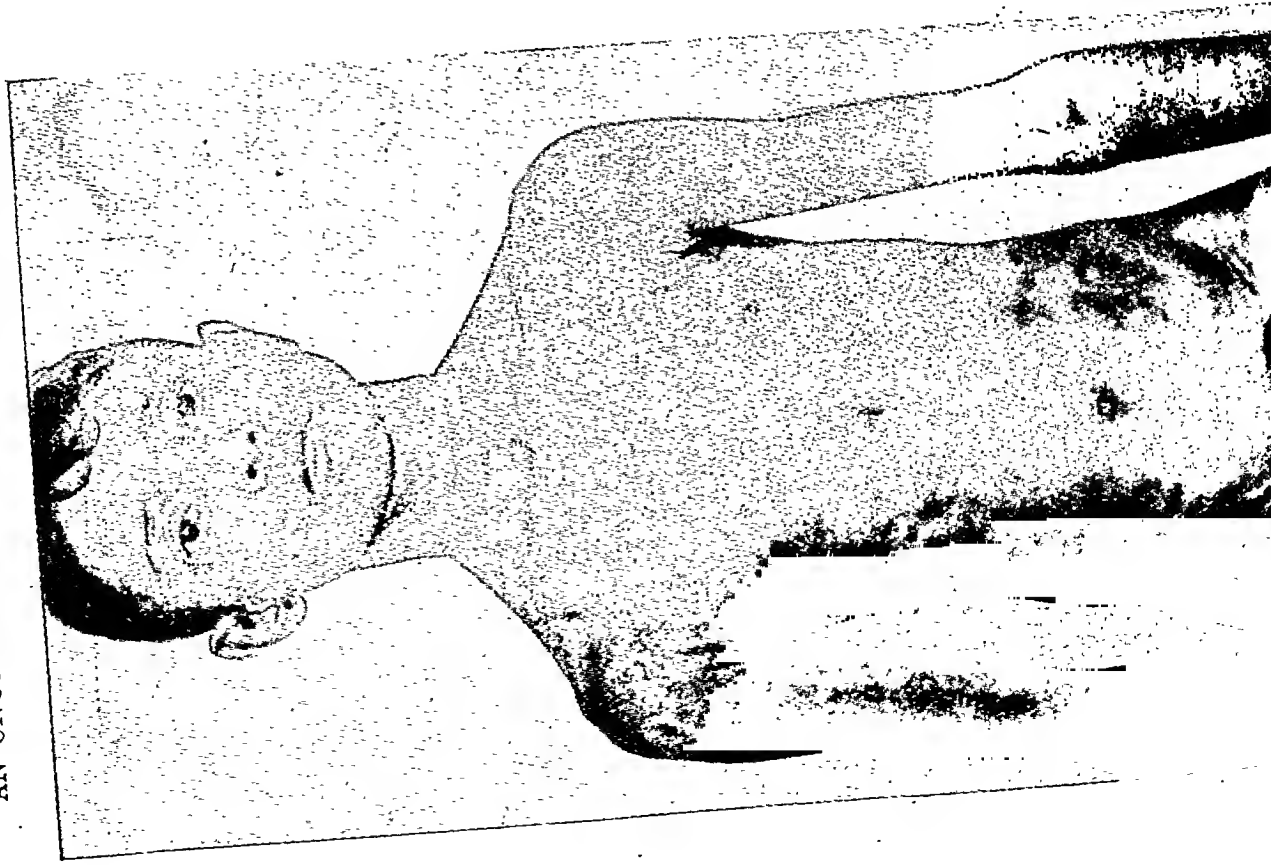


PLATE XXIV

AN UNUSUAL CASE OF POST-KALA-AZAR DERMAL LEISHMANIASIS :
P. C. SEN GUPTA, D. PANJA & A. K. BANERJEE. (O. A.) PAGE 138



AN UNUSUAL CASE OF POST-KALA-AZAR DERMAL LEISHMANIASIS :

P. C. SEN GUPTA,

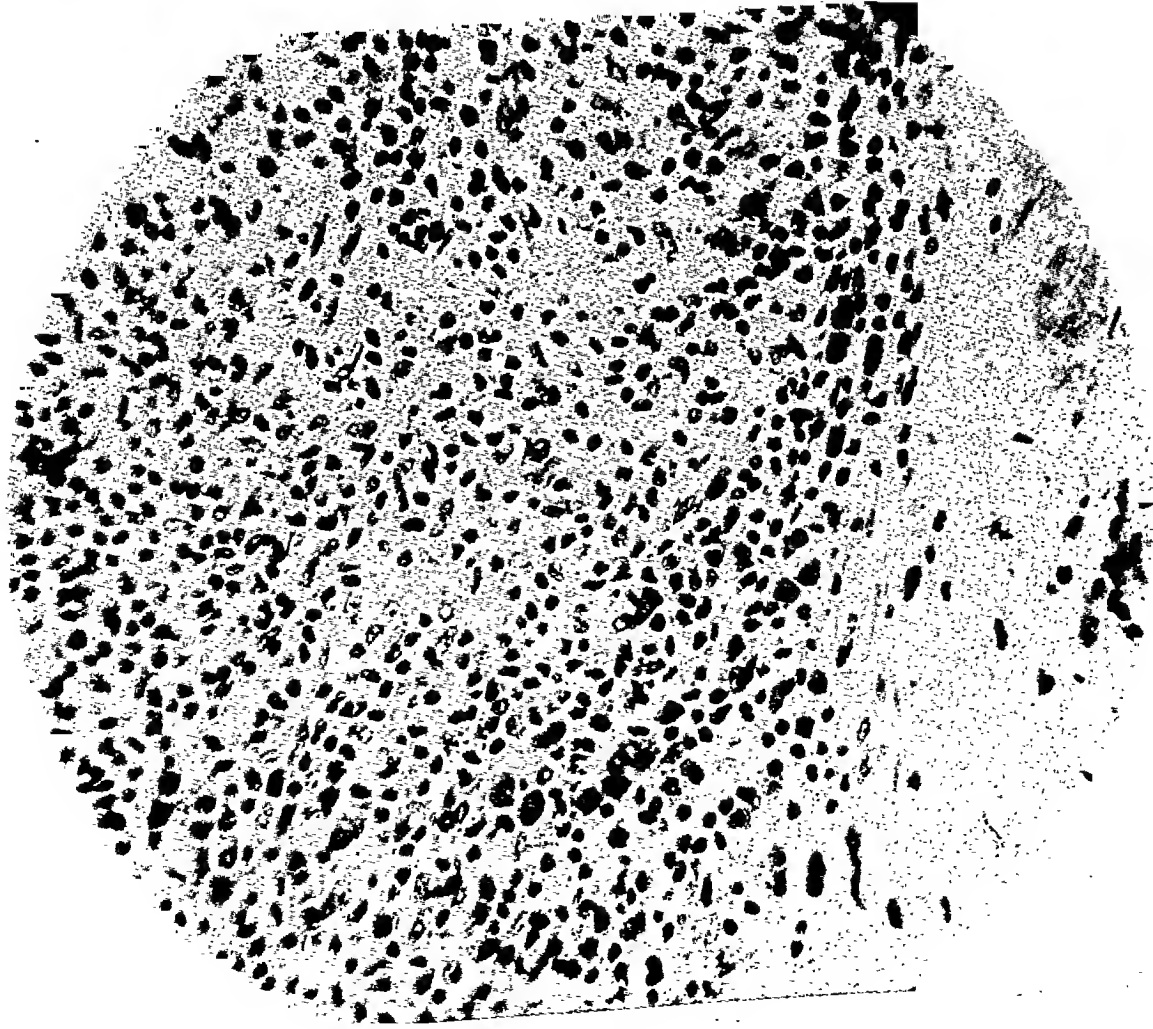
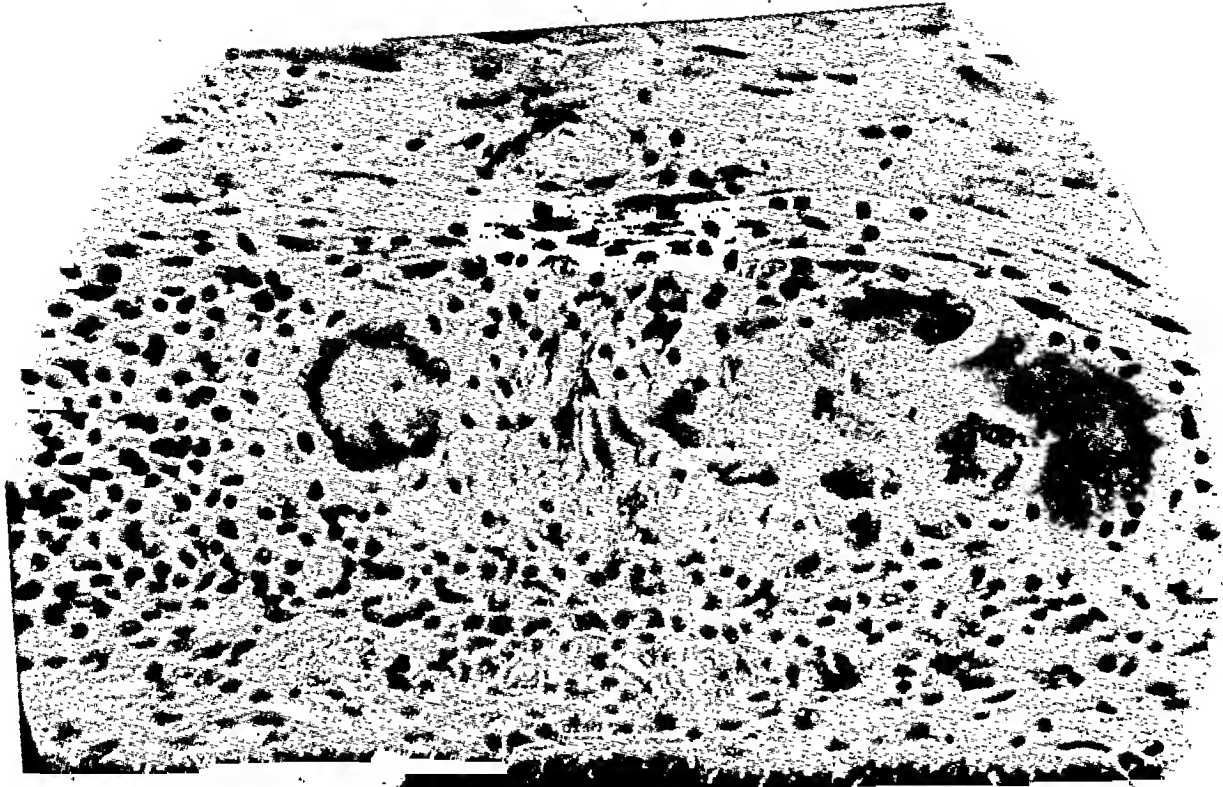


Fig. 5.







Fig. 12.



Fig. 1.



Fig. 2.

Indian Medical Gazette

APRIL

THE HORMONES

THESE substances are secreted by ductless structures and poured into the blood stream for a local or general benefit of the body. The local benefit may be as trivial as the digestion of a special kind of meal needing a special effort on some part of the alimentary canal. A specially liberal portion of cream by its contact with the duodenal surface causes the latter to secrete **CHOLECYSTOKININ** which, through the blood, stimulates the gall-bladder to contract more vigorously and pour more bile into the duodenum to deal with the extra cream. The general benefit may be what makes the difference between a hero and a coward at the spur of the moment, probably an extra supply of adrenalin only (or also of cortical hormone) by the adrenals. The general benefit may also define the well-known human temperaments which make the difference between man and man in the daily conduct of human affairs. The temperament differentiates between the common herd that lives and dies in the social rut and the reformer or the artist who climbs out of the rut, looks round and acts in a manner different from that of the rut dwellers. In all probability the hormones make the superman whose memory defies time and reverence to whom defies racial and geographical barriers.

The ductless structures, also known as the ductless glands, glands of internal secretion, the endocrine glands or simply the endocrines, have been recognized regionally for some time. The hormones can, therefore, be described regionally.

Hormones of the digestive tract : (1) **GASTRIN**.—It is made by the pyloric end of the stomach under the influence of food and stimulates the secretion of gastric juice. It may be only histamine.

(2) **SECRETIN**.—It is formed in the duodenum and stimulates the pancreas to secrete pancreatic juice.

(3) **CHOLECYSTOKININ**.—It is also formed in the duodenum and stimulates the gall-bladder, as has been mentioned already.

(4) **INSULIN**.—It is produced in the pancreas by a group of cells (islets of Langerhans) which do not secrete the ordinary pancreatic juice. It is a protein and consists of a relatively large amount of sulphur-containing amino-acid, cystine.

The present unit causes oxidation of about 2 Gm. of glucose in man. Crystalline insulin has a potency of 24 units per milligram.

Insulin combined with protamine (a simple protein) and known as protamine insulin produces more prolonged effect after injection. Addition of zinc makes the action still more prolonged. One daily injection of protamine zinc insulin will control blood sugar level in many diabetics.

Other hormone-like substances of the digestive tract : (1) **Enterogastrone**.—Fats and sugar entering the duodenum inhibit gastric secretion and motility. The inhibition is brought about by this substance produced by the duodenal mucosa. A deficiency of the substance may be responsible for certain types of gastric hyperacidity and gastro-intestinal ulcers (Selye, 1947). The active substance has not yet been isolated.

(2) **Urogastrone**.—This substance is supposed to originate in the duodenum and small intestine and is secreted in the urine. It inhibits gastric secretion but not motility.

(3) **Anthelone**.—This substance also recovered from urine prevents the Mann-Williamson ulcers in dogs.

(4) **Duodenin**.—Certain duodenal extracts exert a trophic influence on the Langerhans islets and thus produce hypoglycaemia in animals.

(5) **Incretin**.—Certain duodenal extracts stimulate the Langerhans islets and produce more insulin. This effect has been observed in human diabetics also.

(6) **Duocrine**.—This substance also depresses blood sugar.

(7) **Villikin**.—From an acid extract of intestinal mucosa is obtained this substance which stimulates the movements of intestinal villi.

(8) **The anti-anæmia principle of Castle**.—This is the 'Intrinsic Factor' present in the normal stomach mucosa. With the 'Extrinsic Factor' in meat, yeast, etc., it forms in the lumen of the stomach the anti-anæmia principle which reaches the liver for storage. It is released, as required, to stimulate the bone marrow to form erythrocytes. The factor is thus only a part of the hormone usually present in the liver.

Hormones of the thyroid.—This was the first hormone to be recognized and used successfully in cases of deficiency 59 years ago. The name now has settled down to **THYROXIN**, a constituent of the protein thyroglobulin, the main component of the colloidal material which fills the cells of the thyroid gland. The protein is believed to be derived from tyrosine, an

amino-acid. Iodinized protein with properties of the hormone are available.

Hypothyroidism when congenital produces cretinism and when occurring in the adult myxoedema. Both are amenable to treatment with the hormone. The desiccated gland from edible animals by mouth still remains the method of choice.

Hyperthyroidism used to be a difficult morbid state to control. Lately, chemotherapy with thiouracil has made matters easy. In days gone by maniacal symptoms occurring in a case of hyperthyroidism meant the end. Now the patient gets over them easily (Beaumont, 1950).

Radioactive thyroxin is available for controlling hypertrophied thyroid.

Hormone of the parathyroid.—The parathyroid secretion is probably a protein. Its main function is to maintain the normal level of calcium in the blood. The hormone has not yet been prepared in a pure state. Extracts of parathyroids are available for use in tetany.

The hormone withdraws calcium from the bones. In case of hyperthyroidism, due to adenoma of the gland, bones become soft and calcium is deposited in kidneys. The hormone is believed to act on bone osteoclasts and mobilize minerals from them (Cameron, 1947).

Dihydrotachysterol is said to act like the hormone in increasing phosphate excretion (Harrow, 1946; Cameron, *loc. cit.*).

Hormones of adrenals: (1) *From the cortex.*—At least 3 groups are recognized:

(i) Sex hormones. They are (a) Androgens, like the substances produced in the testes, (b) Oestrogens, like the substances produced in the ovaries, and (c) Progesterone, like the substance also produced in the ovaries.

(ii) Carbohydrate hormones. One hormone isolated recently has become a historic event in endocrinology. As *COMPOUND E* or *CORTISONE* (17-hydroxyl-11-hydrocorticosterone), it has given relief in rheumatoid arthritis, rheumatic fever, gout and other collagen diseases, dramatically. A patient who could hardly walk was able to run in 18 hours (Kersley, 1950). The cost of the preparation however is at present prohibitive, £4,000 per patient for two weeks' treatment. The synthesis consists of 35 separate processes used in converting desoxycholic acid in the bile into this wonder drug which has beaten B_{12} of the allied substances, the vitamins, in alleviating human suffering. It is possible to prepare the hormone from plants, *Strophanthus sarmentosus* and yams, also. A British team is touring Africa for the purpose. That India has the same resources does not appear to have been realized yet.

(iii) Electrolytic hormones. They are used in Addison's disease which is characterized by two important changes in metabolism: (a)

excretion of large amount of sodium in urine, leading to its low concentration in blood and high concentration of potassium and (b) fall in blood sugar level. Two important members of electrolytic hormones are (a) *DESOXYCORTICOSTERONE* which corrects the abnormal metabolism of sodium and (b) *17-HYDROXYCORTICOSTERONE* which corrects the sugar level. Both are derived from a sterol nucleus. As a matter of fact there are many commercial preparations and several are prepared synthetically.

For the whole principle of the adrenals the 'Adrenal Cortex Extract' is generally used.

(2) *From the medulla.*—*ADRENALINE* or *EPINEPHRINE* was originally derived from the medulla. It is now made synthetically. It stimulates the sympathetic nervous system, contracts blood vessels and counteracts the mechanism underlying allergy (including anaphylactic shock). Ephedrine, derived from a plant, *Ephedra vulgaris*, has similar effects (compare expectations from *Strophanthus sarmentosus*).

Experimental work on the thyroid and adrenals has suggested an antagonism between them (Long and Miles, 1950).

Hormones of the testis.—*TESTOSTERONE* is produced by the cells of Leydig in the stroma of the testes. This hormone is probably converted into Androsterone and Dihydroisoandrosterone before being excreted in the urine.

The traditional birthday of endocrinology is 1st June, 1889, when the experiment with the testes hormone was described to the Societ  de Biologie de Paris. The famous French physician Brown-Sequard, aged 72, had injected himself subcutaneously with Pasteur-filtered aqueous solution obtained from a suspension of dog's testes. The feeling of rejuvenation described is the best example of subjective feeling (Selye, *loc. cit.*). The aqueous filtrate could have contained no more than a hom opathic dose of a fat soluble substance, far too small for an effect in allopathic medicine.

Testosterone in pure form was prepared much later from bulls' testes (Selye, *loc. cit.*). Synthesis of androsterone from a cholesterol derivative marked a very important advance in the study of sex hormones in general (Harrow, *loc. cit.*), although the method has not yet been employed commercially.

All the preparations are called Androgens, collectively. Their main function is the development of masculine secondary sexual characters such as deepening of the voice, growth of a beard and body hair at puberty. They also control the full development of the glands of reproduction.

Preparations are available for parenteral, per os (sublingual route is better) and percutaneous

uses. They can also be implanted. In the male they have been used in correcting sexual immaturity and treating psychoses in the young, and prostatic discomfort and climacteric (male) in the old (Todd, 1946). They have been also used in curing certain grades of homosexuality. In the female they have been used in inhibiting lactation, in treating chronic mastitis and mammary cancer, in removing frigidity and in correcting uterine disorders which have not yielded to the hormones of the ovary (Robson, 1947; Stephens, 1947; Birnberg, 1949). They have also been tried in angina pectoris (Vakil, 1949).

Hormones of the ovary: (1) *From the developing follicles.*—The follicles during their development elaborate oestrogens. They are steroids and of the same basic chemical structure as the hormones of the adrenal cortex and the testes. α -**ÆSTRADIOL** is considered to be the primary oestrogen. **Æstrone** and **Æstriol** are the end-products and less active in function which consists of imparting a feminine contour to the body and developing the uterus for menstruation. The hormone is probably derived from the granulosa cells of the follicle.

The first oestrogenic concentrate was obtained in 1924 from sows' ovaries. It induced œstrus in sprayed rats and rabbits. Later, urine of pregnant women and pregnant mares supplied the same material. Now synthetic oestrogens, stilboestrol, hexoestrol and dienoestrol, are in general use. They are cholesterol derivatives.

(2) *From corpus luteum.*—The structure left behind after the bursting of the follicle in addition to producing oestrogens now produces **PROGESTERONE** also. This hormone is also a steroid and chemically more related to androgens than to oestrogen. Its action consists in preparing the uterus for pregnancy. If pregnancy does not occur the corpus luteum is replaced by a scar and the supply of the progesterone ceases. If pregnancy occurs the corpus luteum increases in size and supplies the endometrium with the necessary stimulus to grow and lodge the embryo.

Progesterone also develops the acini of the mammary gland and relaxes the pelvic ligaments during pregnancy.

Synthetically the hormone is prepared from stigmasterol obtained from soya bean oil. (Yet another important hormone from a plant.)

(Both the structures producing the hormones in the ovary do so under stimulation from the anterior pituitary gland, the master endocrine of the body.)

Many errors in the female physiology have recently been treated with sex hormones, female and male, used in rotation based on menstrual cycles (Birnberg, *loc. cit.*; Kirloskar, 1949; Swyer, 1950; Editorial, 1950a). They have also been used in treating infection with malaria (Gross, 1949). Cancer of the prostate has been

treated with oestrogens (as mammary cancer has been treated with androgens).

Hormones of the pituitary gland: (A) *From the anterior lobe.*—As many as 15 hormones were described a few years ago. Only 6 have been isolated. A 7th may also exist. They are all proteins. The 6 accepted hormones are: (1) Growth hormone or somatotrophic hormone **STH**. Potent extracts from the anterior lobes of bovine glands have produced remarkable differences in growth in rats and dogs. (2) Gonadotrophic hormone **FSH**, follicle stimulating hormone. This hormone promotes the growth of the follicles in the ovaries in the females and of the germinal epithelium in the testes in the males. (3) Gonadotrophic hormone **LH**, luteinizing hormone. This hormone promotes the growth of the corpus luteum in the female and of the interstitial cells of the testes in the male. It is also called **ICSH**, interstitial cells stimulating hormone. (4) Lactogenic hormone. It is also called prolactin, galactin, mammotropin or luteotrophic hormone, **LTH** (it maintains fully-formed corpora lutea even in the hypophysectomized animals). (5) Thyrotrophic hormone. It has been prepared in a highly stable dry form. It may be responsible for exophthalmos in hyperthyroid activity. (6) Adrenotrophic hormone, also called anterior corticotrophic hormone, **ACTH**. This hormone is antagonistic to **STH** (Birnberg, *loc. cit.*). Recently the hormone has been used in the treatment of rheumatic diseases for stimulating the carbohydrate hormone and thus producing the compound E in the system, instead of giving cortisone (Kersley, *loc. cit.*). The substance produced is now believed to be substance F, slightly different from E (Editorial, 1950b).

The Metabolic Hormone including the Diabetogenic Hormone may be the 7th hormone mentioned above.

The ending trophic was originally tropic and may be found sometimes in current literature or even in books. Trophic is more correct inasmuch as the hormone not only 'turns' on the structure but also helps to 'nourish' it.

In addition to the hormones narrated above the anterior lobe is believed to produce many other substances which influence many other organs and activities in the body. They are best included with the 'Twilight Zone of endocrinology' which attaches many incompletely understood failings in physiology to endocrinology and has been created by the unbridled claims of over-enthusiastic specialists (Hyman, 1947).

It is well worth remembering that in the anterior lobe of the pituitary gland there are only 3 kinds of cells: chromophobes, acidophils and basophils. Their potentialities must be totally different from those of other cells in the body if they manufacture chemicals to enable about 0.25 gm. of the tissue to rule the whole body along strictly codified lines.

Only one hormone, *STH*, appears to have been obtained in crystalline form (Selye, *loc. cit.*) and crystallinity in proteins is not a satisfactory criterion of purity (Cameron, *loc. cit.*). It is likely that many substances isolated in different ways are simply breakdown products of 3 original substances secreted by the 3 kinds of cells.

Incidentally, the relative proportions of the 3 kinds of cells differ in the two sexes. In the female the anterior pituitary lobe is slightly bigger and contains fewer chromophobes, more acidophils and fewer basophils. (The whole gland grows with child-bearing and may exceed 1.0 gm. in weight in multiparas.)

(B) *From the posterior lobe.*—Pituitrin with its threefold action, (i) ability to raise blood pressure, (ii) ability to produce uterine contraction and (iii) ability to promote or suppress diuresis under different conditions of renal activity, is well known. It has been divided into 2 hormones: *ALPHA-HYPOPHAMINE* (*OXYTOCIN* or *PITOCIN* acting on the uterus) and *BETA-HYPOPHAMINE* (*VASOPRESSIN* or *PITRESSIN*). Whole gland (posterior lobe) reduced to snuff is used in the treatment of diabetes insipidus.

(C) *From the intermediate lobe.*—*INTERMEDIN* is present in the aqueous extract of the intermediate lobe (more correctly of the tissue between the two lobes). It has melanophore dispersing effect in frogs and fishes. The action in birds and mammals is not known. Success in the treatment of leucoderma has been claimed but not confirmed (Cameron, *loc. cit.*).

In man intermedin is demonstrable both in the anterior and posterior lobe.

Recently the pituitary gland has been studied in detail in connection with mongolism (Benda, 1947). Congenital defect produces mongols and late defects in childhood dwarfs. The 'bone age' of mongols is less than the real age. The effects on the other systems in mongols are so devastating because no other endocrine functions properly in the absence of a competent master endocrine.

In Simmond's disease the anterior pituitary lobe is destroyed by embolism, thrombosis, hæmorrhage, atrophy, fibrosis, neoplasm, tuberculosis, syphilis or trauma. The necrosis of the anterior pituitary lobe is known to occur in prolonged and difficult labour. The disease is the result of the withdrawal of the pituitary trophic influences and is characterized by a general wasting of the body.

In anorexia nervosa the same general appearance may be produced. Recovery is easy.

Adiposogenital dystrophy (Frohlich's syndrome) in boys and girls is characterized by stress on fatty tissue and genitals. It is usually recovered from at puberty and is probably a functional disorder. In Lawrence-Moon-Biedl

syndrome the defect is deeper (Wechsler, 1947). In Cushing's syndrome (believed once to be due to a pituitary lesion) probably adrenal lesions (tumours — not always found) are concerned.

The syndrome of hypopituitarism has been restudied in males and females recently. Emaciation and progeria do not appear to be essential. Loss of pubic hair is important (Sheehan and Summers, 1949).

In cretins the pituitary glands tend to be enlarged.

Nervous pathways involved in the stimulation of the pituitary gland through the hypothalamus have been suggested. In birds light plays an important part in controlling the pituitary activity and cyclic function of the gonads (Robson, *loc. cit.*).

Placental hormones.—Steroid oestrogenic substances and a protein substance 'anterior pituitary like', *A-P-L*, have been isolated. From the *A-P-L* has been isolated *EMMENIN* which produces oestrus in immature rats. Yet another substance which inhibits the continuance of the normal menstrual cycle is also produced.

The *A-P-L* has also been termed Chorionic Gonadotrophic Hormone or Chorionic Gonadotrophin. This substance is present in the urine of pregnant women and is responsible for the various hormone testes of pregnancy.

The principle in the placenta inhibits prolactin (Routh, 1949).

Other organs believed to produce hormones:

(1) *Thymus.*—*Thymocrescin* was described. Its power to accelerate growth has not been confirmed. There is no definite evidence that a hormone is produced by this gland (Cameron, *loc. cit.*). The gland, incidentally, is associated with status lymphaticus and myasthenia gravis.

(2) *Pineal gland.*—Pineal gland preparations, on injection, produced results opposed to those produced by thymus gland preparations. Both findings are unconfirmed. There is no definite evidence that a hormone is produced by this gland.

Tadpoles fed on the pineal gland of the ox from the beginning of life become translucent for a short period (reminiscent of the pineal eye of *Sphenodon*, which is covered over by a transparent scale—Ritchie, 1944).

(3) *Carotid glands.*—*Carotidin* may be a blood pressure depressant.

(4) *Liver.*—*Heparin* is an anticoagulant active principle of some importance. It has also been prepared from lung, muscle and intestinal wall and is available in pure crystalline form. *Yakriton* is a detoxifying substance obtained from liver tissue. It detoxifies a variety of toxic substances like histamine, urea, ammonia and chloral hydrate. Its hormonal nature has not yet been proved (Selye, *loc. cit.*).

(5) *Kidney*.—It produces *Renin*, an enzyme and a globulin. In the blood stream the enzyme acts upon *Hypertensinogen* (produced in the liver) to produce *Hypertensin*, a vasopressor substance. Ordinarily *Hypertensinase* appears to deal with the situation (see also 'endocrine kidney' below).

(6) *Spleen*.—*Splenin* has been suggested (Cameron, *loc. cit.*). Trauma, hemorrhage, starvation and noxious stimuli may produce an endocrine response involving the pituitary gland, the adrenals and the spleen, and producing the same phenomenon which has been described as 'alarm reaction' (*vide infra*).

All other organs considered endocrine may well be assigned to the aforesaid 'twilight zone of endocrinology'. They include salivary glands, tonsils, adenoids, appendix, prostate, lymph glands, etc., etc.

Other hormones and hormone-like substances.—In addition to the hormones and hormone-like substances detailed in this account there remains yet another group. It consists of: (1) *Histamine*. It is probably formed in the intestine by the action of bacteria on the amino-acid histidine as a routine. In injuries it is formed by the damaged tissue. It plays an important rôle in anaphylaxis and allergy. (2) *Acetylcholine*. It is liberated at the parasympathetic and thoracic sympathetic nerve endings. All the effects of parasympathetic stimulation may be due to it. It produces in monkey the 'fright reaction': contraction of facial muscles after the 7th cranial nerve has been severed. Fright liberates acetylcholine from an unknown source (Selye, *loc. cit.*). (3) *Kallikrein*. It is probably a pancreatic hormone and is a vasodilator. It has been isolated from urine. (4) *Vasotonin*. It is also produced in the pancreas and can be isolated from crude insulin preparation.

Morphological classification of the endocrine glands.—The following types are recognized: (1) *Storage type*. The thyroid is an example. The hormone is stored in special spaces for some time. (2) *Solid type*. The parathyroids are the example. The blood supplies the material for the manufacture of the hormone and removes the previously formed hormone. (3) *Mixed endo-exocrine gland type*. The pancreas is an example. The hormone secretion portion, islets of Langerhans, is solid. (4) *Simple exocrine gland*. The liver is an example. (5) *Non-glandular endocrine organ*. The parasympathetic nerve endings supply an example.

Newer knowledge: (1) *General adaptation syndrome*.—Certain physiological mechanisms raise the power of resistance of the body, to stress or damage, through the endocrinal system (as opposed to the immunological system). Three stages are recognized: (i) Alarm reaction. It produces the signs and symptoms of shock. Gastro-intestinal ulcers are characteristic of the shock. 'Air-raid ulcers' are so produced.

(ii) Stage of resistance. Probably adaptation to one kind of stress or damage is acquired at the cost of lowered resistance to other kinds of stress or damage. (iii) Stage of exhaustion. This stage supervenes when the body has failed in maintaining the required resistance. Diseases of adaptation now develop: among them are hypertension, rheumatic diseases, gastro-intestinal ulcers and diabetes. In the last disease one can visualize in the body a damage area needing for its repair or maintenance glucose which the endocrines set free in the blood for the purpose. The alarm reaction is not a calamity but a necessity in view of the exposures of the body to danger and stress in daily life.

Incidentally, the syndrome may be a link between endocrinology and immunology so far as the stress of infection is concerned.

(2) *A link between vitamins and hormones.*—This is provided by several derivatives of cholesterol.

(3) *Hormones in plants.*—Substances responsible for growth have been isolated from tips of oats, corn, fungi and yeast. Human urine is another such source. Nicotinic acid, vitamin B₆, also affects growth. Ethylene vapour has a stimulating effect on certain parts of plants. Commercially oranges are coloured by exposure to this gas (Harrow, *loc. cit.*).

It has also been held that vitamins (for animals) obtained from plants are hormones for the plants.

(4) *An essential difference between hormones and vitamins.*—Hormones, unlike vitamins, cannot be stored in the animal body. This conception need not go against the vitamins being the plant hormones as metabolism in plants is essentially different from the one in animals, resulting in an excess of anabolism.

Another distinction made is that hormones are produced in the body of an animal but vitamins are taken from outside (ultimately from plants). According to this conception ascorbic acid is a hormone for all animals except primates and guinea-pigs. Human infant can also synthesize it for about the first 3 months.

(5) *Anti-hormones.*—Such was the principle in the milk of thyroidectomized goats. Whether the anti-hormones are true anti-substances of the hormone class or merely antibodies against the vehicle of the hormones, ordinary antigenic substances, is not known. The presumption is that they are merely the antibodies against the vehicles. ACTH from heterogeneous source is likely to become ineffective for this reason alone.

(6) *Fate of the excess of hormones in the body.*—They are destroyed in the body or at least made inert as a rule. The oestradiol, for example, is destroyed in the liver. When the liver is out of order the hormone causes symptoms. The treatment is directed to the liver.

(7) *Telegony*.—This item is not really new but is included because most endocrinologists do not mention it. The race horse Blair-Athol had a very characteristic blaze (white bald face). Mares covered by him bore foals which had the same blaze.

Later, these mares were covered by other stallions but they still bore foals with the same blaze. This is the inheritance of a character from a step-sire.

Of all the explanations given so far the endocrinological one appears to be most rational and runs thus: (i) The blaze was a specially strong character and had a locus in the endocrines. (ii) The foetus inherited the locus. (iii) The locus of the foetus acted on the corresponding locus in the endocrines of the mother and so altered it as to make it like itself. (iv) The altered locus in the endocrines of the mother similarly altered the locus in the endocrines of the next foetus.

The fact of telegony was investigated by Darwin in the case of Lord Morton's mare which had been once covered by a quaga and borne a foal with the characteristic markings of the quaga. Later, she bore foals with quaga markings even after mating with an Arab horse. Considering all possibilities, including atavism, Darwin came to the conclusion that the quaga had altered the mare.

Breeders of pedigree dogs hold a strong belief in telegony: A bitch gone astray, according to them, never breeds true again (Greval, in press).

(8) *Intersexes*.—They are subjects who originally develop as genetic males or females but then change into the direction of the opposite sex by anomalies of the endocrines (Cawadias, 1946; Cameron, *loc. cit.*). Treatment with hormones will succeed in some of them. Some will need psychoanalysis. Others cannot be cured.

Interference in genetics by endocrinology is shown by the preceding two items.

(9) '*Endocrine*' kidney.—In experimental animals an ischaemic kidney is responsible for the production of a hormone-like substance which raises the blood pressure (Hadfield and Garrod, 1947; Selye, *loc. cit.*).

(10) *Trace elements in metabolism*.—As opposed to the 'bulk substances' these substances act almost like vitamins and hormones. Many metals and non-metals act in this way besides acting as bulk substances. Ca so acting controls nerve function. The pharmacological action on the system of the minute quantities of the trace elements taken is not, however, the one commonly relied upon in systems of medicine other than homeopathy.

(11) *Hormones, vitamins, trace elements and enzymes*.—All these subtle chemicals are really linked together.

(12) *Gland grafts*.—Hypertrophied adrenal gland from a patient has been grafted successfully into a patient of Addison's disease (Broster and Hill, 1946).

Incidentally, human testes could be made available for grafting, after thorough compatibility tests, in blood banks in big towns, from young healthy subjects dying of accidents, including executions (Greval, *loc. cit.*). The trouble with the monkey glands was that they were foreign to the system and did not thrive.

(13) The latest discovery in hormones, cortisone, has been mentioned under hormones from adrenals. Its preparation from *Strophanthus sarmientosis* or yams, when accomplished, is likely to revolutionize clinical medicine.

(14) *Glands of destiny*.—Thus have the endocrines been also described (Cobb, 1947). The destiny, however, is not the destiny of 'the moving finger writes; and, having writ, moves on' but of the *karma* guided by the will. The will is of the type which is synonymous with faith which will move mountains.

It is this will which makes desperate cases recover. 'Daughter thy faith has made thee whole' was observed by one of the Healers of human ills.

The will operates by developing the dormant potentialities of the endocrines and the rest follows. The endocrines are the servants, not the masters. The psyche organizes the soma through them for the grim battle of life in the struggle for existence on the drab side of the biological fabric. On the bright side of the fabric the same psyche organizes the same soma through the same glands for a mission in life. The proportions in the bulk and/or activity of the secreting cells are different in the two cases, the master gland advancing or halting growths and processes as required by the strategy or policy of life.

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Special Article

TREATMENT OF EPIDEMIC DROPSY

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and

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Ætiology

A RATIONAL line of treatment for epidemic dropsy must necessarily be based on a proper understanding of the ætiological factors and the metabolic and organic changes produced in the system. After S. L. Sarkar's initial observation (1926) the disease has been reproduced in

human volunteers both with argemone oil and with the incriminated mustard oil in affected areas by Lal *et al.* (1937) and Chopra *et al.* (1939). There is little to doubt that adulterated mustard oil is primarily responsible for the large outbreaks of epidemic dropsy. More recently S. N. Sarkar (1948) has isolated the toxic alkaloid, sanguinerine, from argemone oil and shown its capillary dilating and other deleterious properties in animals. Bailey, Robinson and Staunton (1950) have lately synthesized the alkaloid sanguinerine and dihydrosanguinerine and suggested for it the formula—7 : 8 : 4' : 5'-tetramethoxy-3 : 4 dihydro-1 : 2 benzphenanthridone. The avoidance of contaminated mustard oil is, therefore, the first step in prevention and treatment. It seems, however, probable that there may be some other factor or factors such as nutritional or vitamin-deficiency or consumption of abnormally high amounts of carbohydrate which condition the toxicity (Napier, 1947) and help the production of symptoms. This might explain why some members of a group taking the same oil escape while others develop the disease. Chopra *et al.* (1939) also report the failure of the incriminated oil to produce symptoms in one of the volunteers who took only a limited amount of rice in his diet. Though mustard oil has so far been reported in India as the only article of food adulterated with the products of argemone seeds, the possibility of its presence in other foodstuff, particularly if an epidemic occurs in a community not using mustard oil, should be remembered. Epidemic dropsy has been reported in Africa where no mustard oil is consumed and the cause was found to be adulteration of flour with powdered argemone seeds (Steyen, 1950).

Morbid physiology

The organic change in the system is brought about by a widespread capillary dilatation and proliferation in the skin and the internal organs and the entire pathology and symptomatology of the disease may be built up round this basic disturbance in the capillary system (Acton and Chopra, 1927; Shanks and De, 1931; De, 1933; De and Chatterjee, 1935). Some distinct hæmatological and biochemical changes also occur in the disease. Anæmia is almost universal and it is usually of orthochromic normocytic type due to a depression of erythropoiesis though microcytic or slightly macrocytic anæmia may also occur in some cases (Sen Gupta and Napier, 1940). The white cell count is either normal or slightly raised. There is a shift to the left, in the Schillings or Arneith-Cook count and toxic neutrophils appear in the blood depending on the severity of the disease (Chatterji and Halder, 1935). The eosinophils rise a little but may be considered normal for Indians. The sedimentation rate of erythrocytes is invariably raised due to anæmia and some other factor as the corrected figure (for anæmia) also remains high. The coagulation time is normal (Ray,

1927). The biochemical changes were worked out by Ray (*loc. cit.*), Chopra *et al.* (1935, 1940) and others. There is not much change in total protein but A/G ratio is much altered. Albumin is reduced and globulin raised, rise of pseudo-globulin being more marked. The reduction of surface tension and increase of pseudo-globulin seen in this disease have a parallel in anaphylactoid reaction with which it has some symptoms in common (Chopra *et al.*, 1935). Chopra and De (1937) also demonstrated the presence of histamine in the anterior chamber fluid of cases of epidemic dropsy with glaucoma. These support the belief that there is an over-production of histamine in the system, suggested clinically by the intense capillary dilatation with increased permeability and gastro-intestinal irritation, but further work is necessary before the hypothesis can be accepted. The other biochemical changes are a reduction of serum calcium with rise of plasma chloride and blood uric acid, and in chronic or recurrent cases rise of blood cholesterol. Blood glucose, urea, NPN, creatinine and lipid phosphorus are within normal limits (Ray, 1927; Chopra *et al.*, 1940). The urine gives a strong reaction for indican indicating marked putrefactive changes in the intestine. The pH of blood is normal but its buffer action is reduced (Chopra *et al.*, 1935).

We carried out blood volume and available thiocyanate space volume estimations in a number of cases of epidemic dropsy the details of which will be published later. On comparing the results with the normal figures for Indians, it appears that the plasma volume is raised in all the patients but the blood volume is within normal limits. The changes in plasma volume are due partly to plethora and partly to anaemia, the contraction in the red cell volume being compensated by a rise in plasma volume. The anaemia is therefore absolute and the total haemoglobin quantity and RBC volume in the body are also reduced. The thiocyanate space which is normally one-fifth of the body-weight was increased in all the patients and in some the thiocyanate space was high even after clinical oedema had disappeared indicating the presence of latent oedema though the patients looked apparently all right. The plasma chloride figures in our series have been always high and in view of the rise in thiocyanate space and plasma volume we can conceive of high salt retention in the body. The lowering of albumin is partly compensated by the rise of plasma volume though the colloid osmotic tension still remains low. The rise of globulin is more marked in view of the rise in plasma volume. The study of the changes in plasma and extra-cellular fluid volume gave us an opportunity to assess the value of drugs with greater accuracy.

The above findings do not give a very consistent and clear picture of the morbid physiology in epidemic dropsy. They, however, suggest direct capillary damage by the toxin or

the liberation of a histamine-like body in the course of its interaction with the metabolites. This paralyse the capillaries, stimulates their proliferation, increases their permeability and through the continuation of the process produces the classical picture of epidemic dropsy. There are several factors which contribute to the production and perpetuation of oedema :—

- (1) the osmotic pressure of blood falls due to a reduction of the albumin fraction,
- (2) capillary permeability is increased,
- (3) due to the lowering of blood viscosity the hydrostatic pressure is increased (Chopra *et al.*, 1935),
- (4) albumin probably drains out of the damaged blood vessel into the extra-cellular space and increases the colloid osmotic tension of tissue fluid—actually albumin has been found in aqueous humour of epidemic dropsy in higher concentration than normal, and
- (5) salt retention helps in the maintenance of the oedematous state.

Sarkar (1948) has worked out the poisonous effect of the alkaloid sanguinerine which he believes to be the toxic principle of argemone oil responsible for the symptoms of epidemic dropsy. The alkaloid has been shown to be lethal to animals and to have caused dilatation of the capillaries of the choroid, iris and retina in albino rats. He has demonstrated that sanguinerine interferes with the oxidation of pyruvic acid and leads to its accumulation in the body. Wilson and Ghosh (1937) have also reported increase in the bisulphite-binding substance (B.B.S.) in epidemic dropsy though actual estimation of pyruvic acid has not been done. It would appear from Sarkar's work that the mechanism is almost the same as that of vitamin B₂ deficiency which produces its symptoms by interfering with cell nutrition as a result of the blockage of carbohydrate metabolism at the pyruvic acid stage, with the difference that sanguinerine blocks the sulphhydryl radical of a main enzyme thus leaving therapeutic administration of vitamin B₂ ineffective, while vitamin B₂ acts as a co-enzyme in the oxidation reactions. This would envisage a similarity in the clinical and pathological conditions of epidemic dropsy and beri-beri which, however, is lacking. Further experimental and clinical studies are necessary before the problem can be considered fully elucidated.

Lines of treatment

It is difficult to formulate a rational line of treatment based on the epidemiological observations and the functional and organic disturbance produced in the system. However, it will be necessary to consider the following positive facts in the management of a case :—

- (1) Mustard oil adulterated with argemone oil is the primary cause of the disease. It occurs chiefly in a rice-eating population used to a high carbohydrate, low protein diet.

(2) There is extensive capillary dilatation and proliferation with excessive permeability.

(3) As a result, œdema develops with retention of salt and increase of plasma volume.

(4) The serum albumin and calcium are reduced and blood uric acid and cholesterol (in chronic cases) and serum globulin raised.

(5) The carbohydrate metabolism is probably blocked at the pyruvic acid stage.

(6) Cardiac efficiency is reduced and there is electrocardiographic evidence of myocardial damage (Chopra *et al.*, 1937).

(7) Some degree of anemia is usually present.

(8) The toxin in argemone oil being a cumulative poison is probably present in the body long after its withdrawal from diet. Attempts should therefore be made to eliminate and if feasible neutralize it.

The object of treatment should be to eliminate the causative agent and restore the bodily functions. However, since there is no specific remedy for the disease the treatment is far from satisfactory. We can at best help the natural process of healing and return of capillary tone and afford symptomatic relief to the patient as the occasion demands. Keeping in view the facts mentioned above the following general line of treatment is recommended :—

(1) Mustard oil. It should be omitted from the diet. Theoretically there should be no harm in taking pure mustard oil but traces of argemone oil cannot be detected by the chemical tests* and the possibility of its being contaminated cannot therefore be ruled out.

(2) Rest. The patient should be put to bed to prevent cardiac strain and œdema of legs due to the action of gravity.

(3) Diet. It should be rich in protein with a moderate amount of fat and carbohydrate. Carbohydrate is restricted as its normal metabolism is hampered. A high protein intake will help to restore the blood albumin and its colloid osmotic tension. The diet chosen should preferably be poor in sodium and in the severely œdematous cases no salt for cooking nor extra salt should be used. Neo-selaron (Bayer) may, however, be given as a salt substitute.

The high salt retention in the system tends to maintain the œdema and a salt-poor diet will be of great help in its disappearance. When salt is restricted a moderate amount of fluid may be given. Our usual diet in epidemic dropsy cases consist of

Wheat (atta)	..	6 oz.
Milk	..	1 sr.
Eggs	..	2 only
Orange	..	1 only

Banana	..	1 only
Salt-free butter	..	1 oz.
Chhana	..	4 oz.
Potato	..	2 oz.
Green vegetable	..	8 oz.
Sugar	..	1 oz.
Fish	..	4 oz.
Meat	..	4 oz.
Ghee or vegetable fat	..	1 oz.
(for cooking)	..	150.7 gm.
= Protein	..	221.2 gm.
Carbohydrate	..	126.9 gm
Fat	..	2,695
= Calories	..	

A little rice may be added when the patient is convalescing or is fit to work. For cases with diarrhœa we have to curtail the diet temporarily till it improves. A diet like the following may be used :—

(For cases with diarrhœa)

Barley	..	2 oz.
Chhana	..	2 oz.
Dahi	..	12 oz.
Soft rice	..	4 oz.
Mashed potato	..	4 oz.
Sugar	..	1½ oz.
Orange	..	2 only
1 Fish	..	6 oz.
1 Green plantain (as stew)	..	4 oz.
= Protein	..	74.5 gm.
Carbohydrate	..	219.4 gm.
Fat	..	33.1 gm.
= Calories	..	1,331.1

(4) Vitamins. If we accept Sarkar's view that the pyruvic acid oxidase enzyme is blocked by the toxic alkaloid the administration of vitamin B₁ which is a co-enzyme (co-carboxylase) does not help the process in any way. Clinical results with vitamin B₁ or B₁₂ complex are in general rather disappointing. Vitamins C and P are advocated because of the capillary change and hæmorrhage noticed in the disease. The calcium deficiency mentioned above suggests the use of vitamin D. It appears that no particular vitamin is specific for the condition, but to correct any deficiency (clinical or sub-clinical) that might be present and to prevent their occurrence we give our patients yeast tablets with cod-liver or shark-liver oil and citrus fruit which supply all the vitamins.

(5) Drugs. If the bowels are not moving freely, a saline purgative or laxative will have to be given to keep up its regular action. A mixture is usually prescribed containing diuretin, calcium lactate and the Indian variety of ephedrine (*Ephedra vulgaris*). Diuretics and laxatives are intended to eliminate fluid and probably the toxin from the waterlogged system. If the blood pressure is high it would be better to omit ephedrine. Calcium is indicated to replenish an obvious deficiency.

*The ferric chloride test is preferable as the nitric acid test is non-specific. The former, first introduced by Sarkar (1941) and later modified by Sen (1946), detects argemone oil in a concentration of 0.25 per cent or more.

Ephedra vulgaris contains both ephedrine and pseudo-ephedrine, the latter being a cardiac stimulant. Ephedrine acts through the sympathetic and constricts the arterioles and probably capillaries.

The rise of cholesterol is believed to be compensatory as it tends to make up for the drop in osmotic pressure due to fall of plasma albumin. The cause of rise of uric acid is not properly understood and no special measure is needed for it. The majority of the cases will improve with the above regime. In others one or other of the treatments mentioned below may have to be considered.

Though actual rise in blood histamine has not been demonstrated in epidemic dropsy there are evidences (*vide supra*) which strongly suggest a sustained over-production of histamine in the system. Antihistaminics have been administered on this belief. A few years ago we tried torantil, the antihistaminic drug then available in a few cases with favourable results. Later the newer administered drugs, benadryl and anthisan, were administered to a number of patients who showed a rather slow response to them and a part of the improvement might as well be ascribed to rest and diet. The latest antihistamine phenergan which is believed to be seven times more powerful than anthisan and whose action lasts about 24 hours has so far been tried in only three cases and the results are more encouraging. One of them (*vide case 1*) with marked œdema, flush and cardiac failure derived no benefit from usual treatment, mercurial diuretics and B.A.L. successively but phenergan produced remarkable results with increased diuresis, relief of dyspnoea and improvement of cardiac condition. It will however have to be tried in a larger number of cases before its value can be fully assessed.

Case 1.—An Indian male patient, aged 21, was admitted to the hospital attached to the School of Tropical Medicine complaining of œdema and flush, fever, orthopnoea, loose motions and scanty urine for one month.

Past history: Patient and his mother had swelling of both legs when he was 7.

Family history: 15 members were affected in a family of 40 taking the same food and mustard oil.

On examination: Patient was very ill and orthopnoeic. He had œdema and flush of the whole body, one sarcoid in left axilla which appeared one month before the swelling, tachycardia, water-hammer pulse, shifting of the apex $1\frac{1}{4}$ inches out in 5th space. Marked systolic murmur more at the base than apex with loud pulmonary second sound, palpable tender liver, engorged neck veins and B.P. 145/30. During his hospital stay he had high fever and developed slight hæmoptysis and crepitation in the left lung base.

Blood: hæmoglobin 7.15 gm. per cent, R.B.C. 3.2 millions per c.mm., W.B.C. 6,000 per c.mm.,

neutrophil 76 per cent, lymphocyte 17 per cent, monocyte 4 per cent, eosinophil 3 per cent, E.S.R. 34 (Wintrobe), culture-sterile. Circulation time with calcium gluconate (arm-tongue) 9 seconds. Stool: *Giardia* cyst, *End. nana* cyst, blastocystic hominis, hookworm ova. Urine: no abnormality, sp. gr. 1.020, culture-sterile.

He was first treated with ephedrine, calcium and sedatives with no improvement. One injection of neptal with ammon. chlor. by mouth during this period however produced marked diuresis temporarily.

He was then put on penicillin for the possible pulmonary infection but the temperature and lung signs were not influenced by it. About the end of the 5-day penicillin course he was also given 7 B.A.L. injections 2 cc. each in the course of 3 days. As this also failed to produce any impression on the course of the disease, we stopped other medicines and kept the patient for the next 3 weeks on phenergan 25 mg. twice daily. The response was dramatic. Immediately after commencing the drug the quantity of urine increased and temperature and pulse rate came down. The œdema and flush also disappeared with reduction of body-weight. The systolic pressure fell, diastolic pressure rose and the pulse pressure was restored to normal, the final blood pressure being 120/75. The plasma volume and extra-cellular space volume also came down as he improved clinically. Now he is all right except for the cardiac enlargement with systolic bruit and reduced cardiac efficiency.

Comment.—Phenergan brought about dramatic improvement in the case and restored cardiac compensation without digitalis.

British antilewisite has been shown to protect animals from the toxic effect of sanguinerine by providing the sulphydryl radical with which sanguinerine combines in the body (Sarkar, 1948). If argemone oil is a cumulative poison, as it appears to be, the administration of B.A.L. should on theoretical grounds prevent further damage and rectify it to some extent. We have so far administered B.A.L. to two cases. One of them improved initially with a feeling of well-being and diuresis but it was not maintained. The other case who was seriously ill with cardiac failure actually became worse after a transient diuresis and the drug had to be abandoned after 7 injections. Further work on the therapeutic value of B.A.L. in epidemic dropsy is in progress.

In epidemic dropsy there is no evidence of renal dysfunction and retention of nitrogenous bodies in the blood (except uric acid). Urine often contains a trace of albumin, and hyaline and granular casts are occasionally present. Frank hæmaturia has also been reported. However, in the absence of casts and R.B.C. and more than a trace of albumin it is quite safe to administer mercurial diuretics. In cases where œdema and cardiac embarrassment continue in spite of usual treatment, ammonium chloride by

mouth and mercurial diuretic parenterally give considerable relief by a copious diuresis.

Vitamin P or its analogue Rutin has been tried in the hope that it will reduce the capillary permeability. The results are encouraging but it will have to be tried on a greater number of cases before a definite opinion can be given.

Treatment of complications

(a) Heart failure. Congestive cardiac failure is a common complication of epidemic dropsy and its treatment often creates a problem. In many cases the patient goes progressively downhill in spite of all efforts to restore the cardiac compensation including digitalis therapy. Chopra and Basu (1930) observed that digitalis is not only ineffective but may be distinctly harmful especially in the early stages. They advocate tincture *ephedra vulgaris* which controlled heart symptoms in most of their cases. We estimated the circulation time with intravenous calcium gluconate in a number of cases and this was found to be short even in cases with obvious venous engagement. This raises the question whether the failure is of high output type where digitalis therapy is contra-indicated. The question can be finally settled by the cardiac output estimations and until this is done we have to depend on clinical experience. In our cases of epidemic dropsy with cardiac failure digitalis has given good results in some (*vide* case 2) and failed in others. In marked congestive failure digitalis therapy should be given a trial before discarding it. Tincture *ephedra vulgaris* by virtue of its pseudo-ephedrine content is a cardiac stimulant but it is difficult to see how it can directly help a decompensated heart, though it may be beneficial to some extent. Mercurial diuretics may be helpful and oxygen inhalation, purgatives, venesection (when anaemia is absent or slight) and sedatives will have to be resorted to as required. The salt-poor diet mentioned above should be more strictly followed in the cardiac failure cases. An acute pulmonary oedema may develop and will have to be treated with morphine, atropine, intravenous hypertonic solution, oxygen inhalation and if necessary venesection.

Even after recovery from an acute attack some cardiac disability may persist and requires careful watch and supervision. Many cases, however, become heart conscious and develop cardiac neurosis or neuro-circulatory asthenia.

Case 2.—An Indian female, aged 40, was admitted with the complaints of swelling of the legs, palpitation, breathlessness and scanty urine. The illness started with diarrhoea 4 months ago and gradually oedema and other symptoms appeared.

On examination: She had oedema and flush of both legs, one large sarcoïd over the left cheek, coated tongue, anaemia, engorged neck veins, tachycardia and hurried respiration. Tempera-

ture—normal, blood pressure—140/80. Heart: apex beat in 5th space, a little out; systolic murmur more marked at base. Lungs: N.A.D. Liver and spleen: not palpable. Calf tenderness, knee and ankle jerks present.

Blood: hæmoglobin 5.8 gm. per cent, R.B.C. 2.72 millions per c.mm., MCV 99.2 μ , MCH 21.3 μ , MCHC 21.4 per cent, WBC 7,900 per c.mm., neutrophil 72 per cent, lymphocyte 22 per cent, monocyte 3 per cent, eosinophil 2 per cent, normoblast C 1 per cent, ESR (Wintrobe) observed 38, corrected 24. Van den Bergh test: negative, W.R.: negative. Stool and urine: no abnormality.

Orthodiagram showed enlargement of the left auricle and left ventricle and electrocardiogram revealed no abnormality except sinus tachycardia and sinus arrhythmia.

She was put on tincture digitalis 15 minims 6 hourly. After about a week there was considerable improvement of her condition and digitalis therapy was discontinued. After a few more days she was gravely ill again with congestive failure and moist sounds appeared in the lung bases. She was treated for the next 10 days with intravenous glucose, coramine, vitamins, tincture *ephedra vulgaris* and penicillin. As these failed to improve her condition, she was again put on digitalis (digoxin 0.25 mg. t.d.s.), atropine and omopon for the pulmonary oedema and neptal injection with ammon. chloride mixture. With this regime the cardiac compensation was gradually restored and blood pressure came down to 120/60. She was however given both liver extract and iron for the dimorphic anaemia. As the diarrhoea was exhausting and did not respond to sulphaguanidine, an astringent mixture had to be prescribed. She gradually made complete clinical recovery and on discharge the heart shadow—though still somewhat enlarged—had been reduced in size and only a soft bruit persisted at the base. The sarcoïd on the cheek had shrunk to the size of a pea.

Comment.—Digitalis should be given a trial in all cases of congested cardiac failure.

(b) Anaemia. Usually it is moderate and requires no special treatment. The anaemia improves with general improvement and good diet. If anaemia is marked it should be treated according to the type. Orthochromic normocytic anaemia, the usual type in epidemic dropsy, may, however, require blood transfusion if it is severe or becomes worse in spite of general treatment. Hookworm infection may be associated and requires adequate treatment (*vide* case 1).

(c) Diarrhoea. The diet should be changed as indicated before but it should not be curtailed much or for too long periods. If the diarrhoea is not severe it need not be interfered with and may be left to subside spontaneously. In intractable diarrhoea kaolin or bismuth or other astringents may be used. Sulphaguanidine does not help unless concomitant bacterial infection is present.

The stool should however be examined and any associated infection treated.

(d) Glaucoma. Very high tension is recorded with the tonometer but cupping of the fundus or cedema of the cornea has been reported even in the absence of high tonometer reading. A careful watch should be kept on the visual field and when markedly contracted anterior sclerotomy operation is necessary to prevent permanent loss of sight. Pilocarpine and eserine are not helpful. When the visual field is not much affected no special treatment is required for the eyes which improve with general treatment for epidemic dropsy.

(e) Abortion. Pregnant women with epidemic dropsy almost invariably abort and those who go to full term have still-births. The abortion is due to unhealthy state of the endometrium and placenta which is hæmangiomatous. Histamine contracts the uterine muscle and its over production in the body may be a factor. The non-pregnant women frequently complain of menorrhagia and metrorrhagia. M. N. Sarkar (1935) observed intense capillary engorgement of the ovaries in epidemic dropsy cases where he detected free blood by puncturing posterior vaginal wall and the symptoms were suggestive of ectopic gestation. He finds no risk in surgically handling epidemic dropsy cases with pregnancy. The question is, however, whether pregnancy should be terminated. In general, one should keep the patient under observation and follow an expectant line of treatment, though spontaneous abortion or still-birth is the usual sequel. Probably the best course is to treat the epidemic dropsy and complications arising from it and leave the pregnancy to itself. The patient's relatives should however be warned of the danger of abortion.

(f) Sarcoids. Many of the sarcoids disappear or wither and greatly diminish in size as the patient improves. In the acute stage no interference is necessary unless they bleed. When the patient is free from acute symptoms the nodules may be removed by carbon dioxide snow, ligation or electro-cautery (Chopra and Chaudhuri, 1935).

(g) Fever. It is a common symptom of the disease and no special treatment is necessary for it. If it is too high or tends to persist a thorough investigation should be made for any intercurrent infection and the appropriate treatment given. The nodules may become septic and will respond to sulphonamide or penicillin (local and if necessary systemic).

(i) Hæmorrhages. This may be local from the nodules or piles or systemic hæmorrhage from the mucous surface. Bleeding from sarcoids may be controlled by pressure bandage, application of Russell's viper venom or thrombin topical or electro-cautery. Surgical removal of the sarcoid does not cause any bleeding if it is incised through the healthy skin. Systemic hæmorrhage is not usually severe but if necess-

ary calcium, coagulen, vitamins C and K may be tried and if they fail plasma or blood transfusion will have to be given. Bleeding piles should be treated surgically if local applications fail.

The criteria of cure

It is not always safe to pronounce cure when only cedema, flush, diarrhoea and other symptoms have disappeared. The cardiac disorder often persists much longer and the patient develops breathlessness and palpitation on exertion. The cedema may return a little if the patient is allowed to be up and about too soon after their disappearance. The usual criteria which should be fulfilled before the disease may be considered cured are disappearance of all symptoms including flush and cedema, shrinkage of the sarcoids, return of compensation and heart size to normal and disappearance of murmur. Some enlargement and a soft systolic murmur may however persist for a long time. The diastolic pressure rises, systolic pressure falls and pulse pressure returns to normal. The hæmoglobin, R.B.C. and E.S.R. are also restored to normal values.

Prevention

A disease which can cause high mortality, which can seriously affect the heart and eye sight, and which can cause abortion of pregnant women must be energetically dealt with and not according to the present slipshod methods. It is suggested that strong public health measures be taken to stop the contamination of mustard oil, the cooking medium of a large section of the Indian population, by argemone oil. Arrangements should be made to test the oil supplied to the public and condemn (or make unedible) the consignment containing argemone oil, thereby putting pressure on mill-owners or oil-dealers. This is most important, as the heavy percentage of argemone oil in many samples of mustard oil points to deliberate, and not accidental contamination. Drastic action should be taken in cases of adulteration to prevent this deliberate assault on the health of the people. Imported oil should be received in special centres where chemical examination can be arranged. Supply of sealed tins of 'certified oil' may also be arranged.

Question arises what to do with the large stock of contaminated oil. One would hardly care for the oil which is regarded as deadly poison. There is, however, prospect of freeing the contaminated oil of argemone oil by chemical means (Ray, 1950). If this is substantiated after feeding experiments and if the method be applicable commercially attention may be directed to this method of treatment and the cost borne by the dealer. But we feel that it would be more desirable to prevent the adulteration of the oil than to detoxicate it after allowing it to be poisoned.

The seed that is sent to the oil press should be inspected and all the batches containing

sialkanta seeds condemned, thereby putting pressure on the agriculturists. The method to separate out the argemone seeds from the mixture by virtue of the difference in their density evolved by the industrial engineers is worth consideration (may be applied) to prevent the wastage of mustard seeds.

A move should also be made to exterminate the argemone plants before the seeds ripen. The agriculturists must co-operate in this respect or be penalized. Plants abounding in waste lands should be destroyed by the local authorities. Much can be done in this direction by conjoint effort of the Central and Provincial governments.

As far as an individual is concerned the only advice we can give is to have his mustard oil (a) from a reliable source, or (b) preferably tested by the rough nitric acid test or (c) to use substitutes, e.g. ghee (if available and can be afforded), groundnut oil, til oil, or hydrogenated oil or vanaspati.

Those who have once suffered from epidemic dropsy retain a predisposition to further attacks and should be more careful.

Lastly we may suggest that epidemic dropsy should be made a notifiable disease so that public health authorities may find out the source and take prompt necessary action.

Summary

The aetiology and pathological physiology of epidemic dropsy are discussed—

(d) Others : Biochemical changes in blood—albumin and calcium reduced; globulin, uric acid and cholesterol (in chronic cases) raised; gastrointestinal irritation; complications, e.g. abortion, glaucoma, etc.

Treatment

Keeping the above facts in view the rational treatment of epidemic dropsy is outlined as follows :—

(1) Omit mustard oil to stop further ingestion of the toxic principle.

(2) Rest, specially for the heart.

(3) Diet, high protein with a moderate quantity of fat and carbohydrate, poor in salt.

(4) Vitamins. Yeast tablets and cod- or shark-liver oil and citrus fruit.

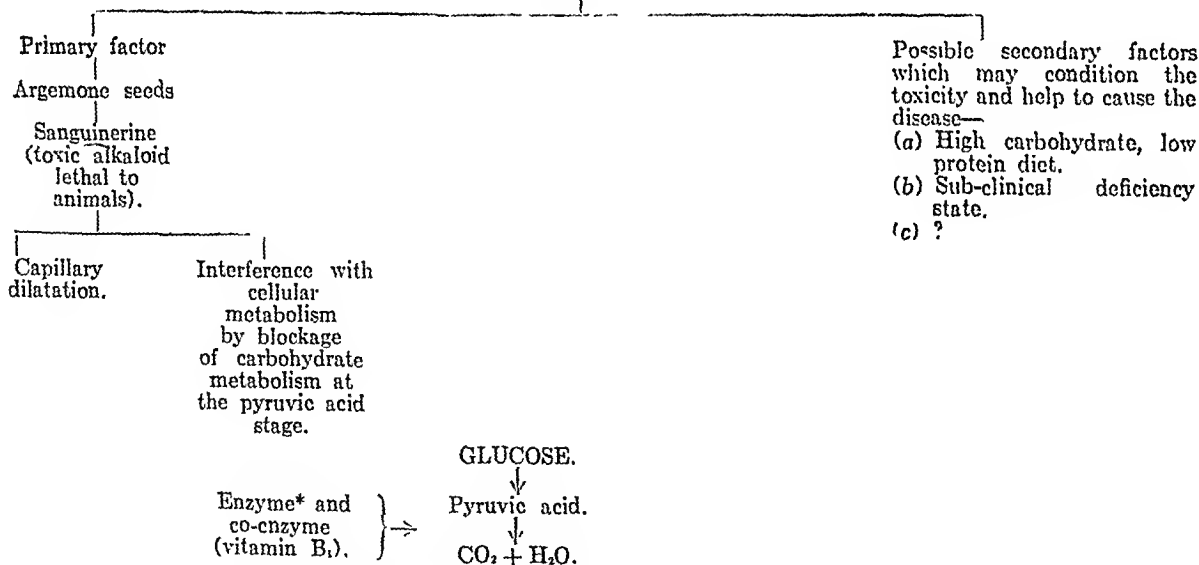
(5) Drugs :

(a) to reduce capillary dilatation and permeability : *Ephedra vulgaris*, calcium.

(b) to promote elimination of toxin and oedema fluid.

(i) diuretics : diuretin, mercurial preparation,

AETIOLOGY



* Sanguinerine is said to block the main enzyme.

Basic disturbances

(a) Widespread capillary dilatation and proliferation in the skin and internal organs with excessive permeability.

(b) Fluid and salt retention and anaemia with increase of plasma volume and extra-cellular fluid.

(c) Reduced cardiac efficiency → enlargement → failure.

(ii) laxatives if bowels are not moving freely.

(c) Newer drugs like antihistaminics, Rutin, etc., are under trial.

(6) Complications are treated as they arise. Heart failure is treated along the usual lines. Digitalis should be tried in presence of congestive cardiac failure. Mercurial diuretics are often very helpful.

(7) Convalescence should always be slow specially if there is much cardiac affection. Graduated exercise.

Prevention

(A) Strong public health measures to ensure distribution of unadulterated oil :

- (1) Testing the oil supplied to the public and condemning (or making un-edible) the consignment giving a positive reaction to the specific test. Imported oil should be received in special centres for the purpose. Sealed tins of 'certified oil' may also be supplied.
- (2) Repeated checks of mills, stockists and occasionally retail dealers.
- (3) Extermination of argemone plants.
- (4) Inspection of seeds supplied to the oil press.

Possibility of separation of seeds and detoxication of toxic oil are discussed.

(B) Individual measures :

Have oil

- (a) from approved source, or
- (b) preferably tested each time, or
- (c) use substitutes.

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Medical News

C. A. BENTLEY, C.I.E., M.D., D.P.H.

News has been received of the death of Dr. C. A. Bentley, C.I.E., M.D., D.P.H., in hospital at Carshalton on 23rd November, 1949, at the age of 76 after a short illness.

A short account of the work of the late Dr. C. A. Bentley in India in connection with malaria is given below :—

DR. C. A. BENTLEY, a close associate of Sir Rickard Christophers, the father of Malaria Research in India, made valuable contributions to the study of this disease. In 1909, Dr. Bentley was appointed Officer on Special Duty to investigate into the causes of malaria in the Island of Bombay and his report, published in 1911, containing as it did concrete suggestions about the method of conducting malaria survey, has served a useful guide for other workers.

About 1911 he was appointed Special Deputy Sanitary Commissioner, Bengal. He early realized the importance of proper distribution of anti-malarial drugs and introduced several schemes of quinine distribution by sales through Post Offices or free, through charitable dispensaries. He also read papers on Quinine

Propaganda at the Third Meeting of General Malaria Committee, Madras, in 1912.

In 1913, he published a report on the Anti-Malaria Operation at Dinajpur, Bengal. The chief interest of the report lies in the fact that it records an attempt to combat malaria in that small town on the lines laid down by Major Sir Ronald Ross, K.C.M., in his report on the Prevention of Malaria in Mauritius. Briefly, the measures adopted consisted in 'case reduction' by the distribution of quinine, and 'mosquito reduction' by means of 'minor measures'; and the general principle 'minor works before major works', laid down by Ross in regard to mosquito reduction, was strictly followed. At the All-India Sanitary Conference in 1914, he read a paper on Anti-Malaria Sanitation specially suitable for Bengal.

In his capacity as Director of Public Health, Bengal, to which position Dr. Bentley later rose, he paid considerable attention to the study of malaria in relation to agriculture. In 1925, he published a valuable report entitled 'Malaria and Agriculture in Bengal', which deals with the effects of defective embankments on the incidence of malaria and the huge resultant loss in agricultural production. The conclusions arrived at by him can be summarized as follows:—

(i) Apart from the application of specific measures directed either against the malaria parasite or the anopheline carrier, there is an immense field for the carrying out of anti-malarial projects based upon the principles underlying Italian 'Bonificazione', which embodies measures designed for a double purpose, viz, to improve agriculture and improve health simultaneously.

(ii) The particular type of bonification required in Bengal was Irrigation. This was something new. At one time everybody thought that drainage was what was needed. But experience had shown that agricultural drainage schemes might be very dangerous expedients in Bengal, sometimes doing harm rather than good. All the evidence showed that what was most needed in Bengal was a large increase in the available supply of moisture. He said 'Irrigation must be the watchword of Bengal rather than Drainage'.—J. S.

WORLD HEALTH DAY, 7TH APRIL, 1950. PLAGUE CAN BE ERADICATED BY THE EXPERT ADVISER ON PLAGUE AT THE S.-E. ASIA REGIONAL OFFICE OF W.H.O.

(From a Release dated March 1950 issued by W.H.O.
Regional Office for S.-E. Asia)

THOUGH no more counting its victims in millions as was the case in past times, particularly at the time of the 'Black Death' in the fourteenth century, plague remains a serious menace over wide areas in South-East Asia, China, South America and Africa. In fact, it was less than sixty years ago that this infection which appeared to be quite insignificant at the time, became rampant in Canton and Hong Kong and spread from there not only to the above-mentioned regions but to most other countries of the world as well. Fortunately, however, its ravages remained limited as compared to the havoc caused in historical times and it is now possible to attack the scourge with the newly forged weapons of modern medical science.

Intensive research in India particularly shed light upon the causes of plague, establishing that the infection is perpetuated amongst the rodents, specially the rats, and spread from them to man through the rodent fleas. Thanks in the first line to the labours of the Haffkine Institute in Bombay, vaccines to protect man against the disease became available.

It is, however, only within the last ten years that so much further progress has been made as to render plague a fully controllable disease. Sulfonamides and streptomycin now enable us to save the lives of most victims. Improved methods of prevention by dealing with the rats have been evolved and DDT has been fully efficient in destroying rat fleas and thus cutting short the chain of infection leading from the rodents to man.

The problem facing public health workers now is not so much to search for new methods of controlling or, one can honestly say, of eradicating plague. The essential is to take full advantage of the available effective procedures. However, this battle against an inveterate and treacherous foe of mankind can be won only if the efforts of the medical workers are reinforced by the whole-hearted co-operation of the people.

Since plague is essentially a rodent infection, it almost invariably appears among these animals before human beings are attacked. Hence, if an increase in the numbers of dead rats is noted and reported by the people, the spread of the disease to man can be easily prevented through DDT application and action against the rodents themselves.

Unfortunately, however, the people often neglect to inform the health authorities early enough. Likewise they often fail to avail themselves of anti-plague inoculation which forms a valuable second line of defence.

It is clear that cures obtained by using sulfa drugs and streptomycin will be most certain (amounting to practically one hundred per cent) when treatment is started early, yet often the sufferers at first do not seek adequate help, and are too late in reporting for proper aid.

To change this attitude of the people through public health propaganda and health education is therefore one of the main tasks of modern plague control. The most important ways in which anybody could and should take part in this vital work are summarized below:

What can you do against plague?

- (1) *Plague is caused by the rats—give no shelter to them.*
Keep your house free from rubbish and old unnecessary things.
Store all necessary goods on supports so that the rats cannot hide underneath or behind.
- (2) *Plague is caused by the rats—do not feed them.*
Keep your food in solid covered containers or hang it up so that the rats cannot get at it.
Clean your cooking and eating utensils at once after the meals and put the useless waste into a refuse box which the rats cannot enter.
- (3) *Get inoculated against plague.*
- (4) *Quickly report if you find dead rats in or near your house.*
- (5) *Get proper treatment as soon as symptoms of plague appear.*

BABIES' 'SUFFOCATION' OFTEN WRONG DIAGNOSIS

(Reproduced from Release No. P/1404 issued by the Public Relations Officer, Australian High Commissioner's Office, Connaught Place, New Delhi)

MOTHERS who live in fear of their babies suffocating in their cots will be comforted by the findings of Dr. Keith Bowden of Melbourne, Australia.

Dr. Bowden has discovered that many babies that were found dead in their cots and were thought to

have suffocated in the bed clothes, were in fact victims of natural disease.

In an article in the *Medical Journal of Australia*, Dr. Bowden states that he studied 40 unselected autopsy cases of babies suddenly dying in bed. A primary diagnosis of 'accidental suffocation' had been made in 24 cases.

Microscopic examination in most cases revealed some previously undiscovered natural disease. Inquiry into medical histories showed that many children were not in perfect health before death.

Typical case is that of a child who was found dead face downwards in its cot. This suggested suffocation because the parents thought the child was perfectly well. Routine microscopic examination revealed acute bronchitis and acute heart trouble.

On what evidence is the diagnosis of accidental suffocation by the bed clothes made?

An apparently well baby is found face downwards dead in his bed. He is livid. There is pallor about the face. The heart and the veins may be full of dark fluid blood. There may be froth in the bronchial passages.

This is a picture found in suffocation, but it is a picture found in disease states as well.

The natural tendency of most babies who can move freely is to turn over onto their faces to sleep. If some of them should die of unsuspected natural disease, it is therefore to be anticipated that they will be found dead face downwards.

Dr. Bowden points out that most healthy babies can look after themselves if normal care is exercised in putting them to bed. Their capacity for yelling when in trouble is an excellent safety valve.

Dr. Bowden says it is only by getting rid of the myth of accidental suffocation that parental fussiness, and even tragedy, can be avoided. The stigma attaching to a diagnosis of 'accidental suffocation' may have a serious effect upon the mother.

Dr. Bowden cites a case of one mother who was afraid to go out on the street lest other women should say something implying maternal carelessness. Another mother committed suicide.

In an American magazine recently there was an article stating that '30,000 babies die each year in America from accidental suffocation'. A society has been formed for the prevention of accidental suffocation.

Dr. Bowden suggests that a society for the performance of complete post mortems would greatly reduce these exaggerated figures.

INTERNATIONAL SOCIETY OF HÆMATOLOGY— CAMBRIDGE CONGRESS—21ST-26TH AUGUST, 1950

THE International Society of Hæmatology will hold a Congress at Cambridge from 21st to 26th August. It has been provisionally decided that the programme will be arranged under the following main headings:—

Tuesday	.. The Therapy of Anæmias. Hypersplenism.
Wednesday	.. Leukæmia. Review of Therapy of Leukæmia.
Thursday	.. Physiology and Pathology of Coagulation.
Friday	.. Immuno-hæmatology.

Each session will be opened by one or two invited speakers of international repute. Other contributions will be limited to 10 minutes' duration. Ample time

will be allowed for discussion. Space will be available for scientific demonstrations which may, if desired, be independent of any paper read at the meeting.

Any who wish to read a paper within the scope of the general headings outlined above or to give a scientific demonstration should submit their requests forthwith to the Congress Secretary (Dr. M. Hynes) in order that the Programme Committee may make their selections. The language in which the paper is to be given should be stated. It should be noted that the programme will be co-ordinated and planned by the Programme Committee and that the submission of a request does not guarantee acceptance. Preference will be given to new work rather than work previously published. Requests must be received by 1st March, 1950.

Accepted speakers will be required to forward a précis of their papers to the Congress Secretary in advance, so that translations in English, French and Spanish may be included in the official programme.

Those who wish to attend, should apply to:—

Dr. Martin Hynes,
Department of Medicine,
University of Cambridge,
Cambridge.

MEDICAL PHOTOGRAPHY

AN Exhibition of Medical Photography will be held from 12th to 24th June in London under the sponsorship of the Royal Photographic Society. The Exhibition is open to medical photographers, amateur or professional, throughout the world. Information and application forms may be obtained from:—

The Honorary Secretary,
Medical Group,
Royal Photographic Society,
International Exhibition of Medical Photography,
16, Princes Gate,
London, S.W.7.

REGISTRATION OF DENTISTS: TIME LIMIT TO BE EXTENDED

(From a Press Note dated 8th April, 1950, issued by Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta 7)

THE Dentists Act, 1948, came into force in the whole of India, except Part B States, with effect from 29th March, 1948. Under section 49 of the Act, no person who has not been registered as a Dentist can practise Dentistry after 28th March, 1950, without incurring the penalty mentioned in U-section (2) of section 49 of the Act. Also, under section 46(3) it will not be lawful for a person who is not registered in Part A of the State Registers of Dentists, except with the sanction of the State Government concerned, to hold any appointment as Dentist in any Dispensary, Hospital or other institution in the State which is supported wholly or partially from public or local funds.

The Government of Madras have requested the Government of India to promote legislation to amend section 49 of the Dentists Act so that the time limit mentioned in that section may be extended by another year as the State Dental Tribunal has not yet been able to finish the preparation of the first Registers under the Act. In Bombay the date for registration has been extended to 20th May, 1950, and the Bombay Government have intimated that it will take some months after that date for the publication of the first Register. The Government of India have ascertained

that due to unforeseen circumstances it has not been possible so far in the other States also to publish the first Registers under section 32 of the Dentists Act. In the circumstances, the Government of India have decided to promote legislation to amend section 49 of the Act to extend the time limit mentioned in it by one year as recommended by the Government of Madras. In the meantime, the State Governments have been requested not to initiate any prosecution for the violation of section 49 of the Dentists Act.

PRESIDENT TO OPEN FUEL RESEARCH INSTITUTE: THIRD IN CHAIN OF 11 NATIONAL LABORATORIES. PHYSICAL AND CHEMICAL SURVEY OF COALS

(From a Release dated 10th April, 1950, issued by the Press Information Bureau, Government of India)

THIRD in India's chain of 11 National Laboratories, the Fuel Research Institute at Digwadih (Dhaubad) in Bihar is due to be opened on 22nd April, 1950, by the President, Dr. Rajendra Prasad. The National Chemical Laboratory and the National Physical Laboratory were opened in December 1949 and January of this year by the Prime Minister and the Deputy Prime Minister, respectively.

India has large supplies of iron ore. Her supplies of coking coal, however, are not overabundant. The efficient utilization and conservation of these, besides research into the up-grading of coking coal by mechanical processes are therefore of considerable importance.

In 1928 and 1936 Coal Commissions urged the scientific investigation of these problems—a third commission expressed similar views in 1946—and a Fuel Research Committee was constituted in 1940. It recommended the establishment of a Central Research Station; and Dr. S. S. Bhatnagar, Director of Scientific and Industrial Research, proposed to Government the establishment of the Fuel Research Institute as one of the national laboratories in the country's post-war development programme. The Government of India accepted this recommendation and awarded grants for the purpose in 1944.

20-YEAR DEMAND

The Institute, which is the result of a demand that has been persistent for more than 20 years, will conduct research on major problems concerning fuel—solid, liquid and gaseous—and will operate a physical and chemical survey of Indian coals, the object being to provide a reliable assessment of the quality and quantity of the various coal resources of the country in order to ensure that they are utilized to the best advantage.

In addition to problems of fundamental and applied research, sampling and analysis of coal will be undertaken and pilot-plants are to be developed for various processes.

The Institution's work will be distributed among the following main divisions: Coal Survey and General Analysis; Carbonization and by-products; Liquid fuel (including hydrogenation, synthetic fuels, petroleum and substitutes); Physics (including X-Ray and Spectroscopy); Gaseous Fuels (including gasification); Engineering (including preparation of coal for the market, coal-washing, boiler plant and combustion engineering).

TEMPORARY LABORATORY'S WORK

For three years, work has been conducted in a temporary Laboratory at Dhanbad, where it has been possible to make a beginning on the physical and chemical survey of coals, to study the washability of

many of the seams of the Jharia, Raniganj and Bokaro coalfields, and to undertake preliminary investigations into the carbonization of Indian coals. In addition, attention has been given to the manufacture of synthetic oil by the Fischer-Tropsch process, laying the foundations of sound sampling, analytical, and testing technique and to train a number of fuel chemists.

About 300 samples of coal have been analysed for their physical and chemical properties, such as screen analysis, proximate analysis, ultimate analysis, caking index and calorific value. In some cases, Gray-King carbonization assays of coal and determination of fusion ranges of ash have been undertaken.

MODERN SERVICES AND SUPPLIES

The new laboratories of the Fuel Research Institute have been provided with some of the most modern services and supplies, sight not being lost, however, of the requirements of local conditions. For instance, all the laboratories are air-conditioned, refrigerative cooling being adopted because of the high degree of humidity during the summer and monsoon seasons. Some of the laboratories contain furnaces; others none. Care has also been taken to prevent the noxious fumes from one laboratory being discharged into another. For this purpose a central refrigerating plant with chilled water 'weather-makers' has been installed. From this plant, which employs ammonia as the refrigerating medium, and is of 108 tons capacity, chilled water is supplied in heat insulated pipes to the weather-makers installed in each room. These weather-makers are capable of adjustment to give adequate temperature and humidity control. They also provide the necessary make-up air which is previously filtered, cleaned and cooled. This system prevents conditions in any one room from affecting those in another.

In general the laboratories themselves are on a unit basis, each unit or room accommodating two research workers and two assistants. Walls dividing the laboratories are of comparatively light structure and easily removable, so that should it be desired to convert two or three rooms into one large laboratory, the change-over can be effected with ease. There are steel-framed windows, large enough to allow adequate day-light. For artificial illumination, tubular fluorescent lighting has been provided.

FUME CUPBOARDS

The rooms have been equipped with large fume cupboards, partitioned so that one section is reserved for dangerous fumes. Each cupboard, the ventilation of which has been so designed as to avoid consumption of the conditioned air of the room, is provided with supplies of water, gas, electricity, compressed air and vacuum. It is lighted from above by external fluorescent lighting through a reinforced glass top. Consequently, each cupboard is really a working bench for many purposes.

The Institute's water supply is drawn from a well 15 feet in diameter and 120 feet deep. Water from this well is pumped into a receiver in which the pressure is developed by means of 'entrapped' air. This system is economical and makes unnecessary the construction of a water tower.

The Director of the Institute is Dr. J. W. Whittaker, who will be working in consultation with Dr. S. S. Bhatnagar.

COAL SURVEY STATIONS

There will be six Regional Coal Survey Stations working under the Institute. These are essential for the physical and chemical survey of coals and will be located at the Raniganj Coalfield, with a laboratory near Disbherghar; the Jharia field with its laboratory at the Central Institute at Digwadih; the Bokaro-Ramgarh-Karanpura fields with a laboratory at Ranchi; the Eastern States coalfields (Vindhya Pradesh) with a laboratory at Umaria, Sagra Estate;

The Madhya Pradesh (C. P.) coalfields, with a proposed laboratory at Kamptee, near Nagpur, and the Assam coalfield, proposed laboratory at Dibrugarh.

The Raniganj and Jharia survey stations are already in operation. The others are in the planning stage, but are expected to begin work shortly.

The Coal Survey aims at the systematic physical and chemical examination of coal seams as they exist in the unworked state and of commercial grades of coal as they are produced at the mine. Much information has been collected and classified to assist in the planning of each survey.

With the inauguration of the Jharia Coal Survey a systematic examination of No. X and No. XI seams of the Jharia coalfield has been undertaken. Foot by foot seam samples and commercial samples are analysed and tested for their coking properties, the nature of ash and washability. These two seams constitute a large proportion of the reserves of coking coal in the field.

In the Raniganj field a systematic survey of the eastern end of the area has begun. The suitability of these coals for synthetic oil will be studied.

In the Bokaro field, investigation of the Bermo seam has been undertaken at the request of the Damodar Valley Corporation.

Much preliminary work has already been carried out on Madhya Pradesh (C. P.) coals, involving studies on carbonization, washability and chemical composition.

INDIA AWARDS SEVENTY SCHOLARSHIPS

THE Government of India will award seventy scholarships this year to students from Asiatic and African countries. The grants will be for study in India of the arts and humanities, science, agriculture, medicine, technology, education and law. The scholarships are to encourage international cultural relations, and to provide educational opportunities to students in countries where they are less available. Each grant is of 200 rupees (\$42.08) a month.

Scholarships will be granted to non-Indian students in Indonesia, China, Nepal, Afghanistan, Iran, Egypt, South Africa, Donya, Uganda, Tanganyika, Zanzibar, Malaya, Burma, Ethiopia, Ceylon, Siam, Bhutan, the Philippines, Indo-China, Tibet, Turkey, Portuguese Africa, Mauritius, Nigeria, and to students of Indian origin in South Africa, British East Africa, Ceylon, Malaya, Mauritius, Jamaica, Trinidad, British Guinea, Fiji, Siam, Surinam (UNESCO).

LABELLING PROVISIONS UNDER DRUGS ACT : RIGID ENFORCEMENT TO START IN JULY

(From a Press Note dated 6th April, 1950, issued by Press Information Bureau, Government of India)

THE provisions of the Drugs Act, 1940, and the Drugs Rules, 1945, are being enforced in the country from 1st April, 1947. The labelling provisions under the Drugs Act and Rules in respect of drugs (both pharmacopœial and non-pharmacopœial) imported into or manufactured in the country are, however, being enforced only from 1st April, 1949. The effect of this is that the import and manufacture of drugs, not labelled in accordance with the Drugs Act and Rules, are not being allowed from 1st April, 1949.

Apart from the stocks imported into or manufactured in the country after 1st April, 1949, there are at present in the market unexpended stocks of patent and proprietary medicines and other drugs, imported into or manufactured in the country before the above date, which are not labelled according to the Drugs Act and Rules. As rigorous enforcement of the

labelling provisions in respect of such drugs with effect from 1st April, 1949, would have resulted in considerable financial loss to the trade, time was given to the trade to dispose of such stocks up to the end of December 1949. In view, however, of representations received from the trade that it has not yet been possible to dispose of the entire stocks of such defectively labelled drugs, it has been decided to allow the trade a time-lag of further six months to dispose of such stocks. All stocks of such drugs should be disposed of before 1st July, 1950, from which date labelling provisions under the Drugs Act and Rules will be rigidly enforced in respect of all drugs irrespective of the fact whether they were imported or manufactured in the country before or after 1st April, 1949.

HEALTH MACHINE INVENTION CURES DIVERSE COMPLAINTS. AUSTRALIAN APPARATUS EXPEDITES BLOOD CIRCULATION AND TONES UP SYSTEM. BY CHARLES LYNCH. PHOTOGRAPHS BY JACK GALLAGHER

(Reproduced from Release No. P/1424, The Public Relations Officer, Australian High Commissioner's Office, Connaught Place, New Delhi)

A NEW type of health machine based upon comparatively simple principles, invented by a school teacher in Melbourne, Australia, has created much local interest, as publicity is being given to a wide range of cures for various ailments effected after treatment by the machine.

The inventor calls his apparatus the Glafford neuro-tone, for directional percussion and surge, and it applies massage to various parts of the body by means of a revolving, rubber-lined cylinder.

The apparatus is contained in an 18-inch cube box, and is powered by a $\frac{1}{2}$ h.p. electric motor. The roller attachment revolves at a great speed, and when a portion of the body, such as a leg or an arm is applied to the roller, the latter creates a massaging effect. Vibrations, combined with the sensations created by the moving rubber, cause an increase in the blood surge, and have the general effect of toning up muscles and nervous system. The treatment can be applied to any part of the body, as the inventor has designed and constructed a table with adjustable heights, so that the patient, whilst lying down, can move himself into position to allow the roller to operate on any portion of his body.

The suction properties of sponge rubber are well known and blood circulation is benefited generally as a result of the applied application from the machine. The latter has a slight humming vibration caused by the motor, but it is quite suitable for installation in a bedroom or bathroom for self-treatment, and self-massaging.

The inventor, Mr. Lester Glare, is an ex-serviceman of World War II, and was discharged from the Army as medically unfit, suffering from acute malaria and other complaints. He determined to solve his own physical problem, and to avoid operations recommended by Army doctors. He studied elementary physiology and physical training, and finally evolved the idea of the new machine. With his own treatment he re-built his frail body 'brick by brick', until to-day he is a marvel of physical fitness, with firm flexible muscles, and increased chest measurement.

Complaints which have been successfully treated by the machine include catarrh, indigestion, rheumatism and adjusted bad postures in school children.

A three-year-old case of Potts disease was also treated. Symptoms were hypersensitive nerves, near

paralysis of the limbs, and a discharging abscess below the right ear. After three treatments the abscess freely discharged and then cleared, and healed without a trace.

A certain type of nasal catarrh responds after one treatment, and deafness from the complaint disappears.

Mr. Glare states that positive success has been achieved with sciatica and fibrositis with the machine, plus manipulation, self-treatment and exercise.

One case of long-standing polio is being treated, but the inventor states that it is too soon to form an opinion.

Mr. Glare teaches mathematics at the Hughesdale Technical School and when classes are finished hurries home to a caravan in a yard he has rented, and there treats his patients, the number of whom is increasing as reports of the benefits of his treatment continue to circulate.

He has taken out a provisional patent for his machine.

THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

The following students were declared to have passed the D.T.M. examination, session 1949-50 :—

Passed

(Arranged in alphabetical order)

Dharma Vrata Agarwal, M.B., B.S. (Agra), Private Practitioner.

Nareish Chandra Bose, L.M.F. (Dacca), Assistant Medical Officer, Surguja, C. P. and Berar.

Prem Chandra Bhalla, M.B., B.S. (Bom.), Private Practitioner.

Sailendra Kisor Bhattacharjee, L.M.F. (Dacca), M.B. (Cal.), Private Practitioner.

Sailes Chandra Bhattacharyya, L.M.F. (Dacca), L.T.M. (Cal.), M.B. (Cal.), Private Practitioner.

Bishnu Pada Biswas, M.B. (Cal.), Private Practitioner.

Samir Kumar Biswas, M.B. (Cal.), Private Practitioner.

Jitendra Nath Chakrabarty, L.M.F. (Bengal), Assistant Medical Officer, Satali T.E.

Sunit Chermisrivathana, M.B. (Bangkok), Assistant Worker, Pathology Department, University of Medical Science, Bangkok.

* Ratan Chand, L.S.M.F. (Punjab), Private Practitioner.

Hari Pada Chattopadhyaya, L.M.F. (Bengal), Assistant Medical Officer, Sialkota T.E., Assam.

Masaddarali Chowdhuri, L.M.F. (Dibrugarh), Assistant Medical Officer, Assam Oil Co., Ltd., Digboi.

Nareish Chandra Das, M.B. (Cal.), Private Practitioner.

Radhika Gobinda Das, L.M.F. (Bengal), L.T.M. (Cal.), Private Practitioner.

Prabha Shanker Dave, L.M.F. (C. P.), Private Practitioner.

Satyendra Kumar Dhar, L.M.F. (Bengal), Assistant Medical Officer, Kuttal T.E., Assam.

Satya Pal Dua, L.S.M.F. (Punjab), M.B., B.S., Private Practitioner.

Suraj Mal Dugar, M.B. (Cal.), Private Practitioner.

Sudhir Chandra Dutta, M.B. (Cal.), Private Practitioner.

Anil Kumar Guha, M.B. (Cal.), Private Practitioner.

Prem Kumar Jain, M.B., B.S. (Patna), Private Practitioner.

* Awarded the 'Chunilal Bose' Gold Medal, 1950.

Gholam Mohiuddin Jilani, M.B. (Cal.), Private Practitioner.

Gopal Chandra Kanjilal, M.B., B.S. (Patna), Private Practitioner.

Gurbachan Singh Koelhar, L.S.M.F. (Punjab), M.B. (Cal.), Private Practitioner.

Jai Dev Singh Kohli, L.M.S., P.S.M.F. (Punjab), Private Practitioner.

Satyendu Kumar Kundu, B.Sc., M.B. (Cal.), Private Practitioner.

Mano Har Lal, L.S.M.F. (Punjab), Private Practitioner.

Sambhu Nath Mal, L.M.F. (Bengal), M.B. (Cal.), Private Practitioner.

Hare Krishna Mitra, M.B. (Cal.), Private Practitioner.

Sibnath Mukherjee, M.B. (Cal.), Private Practitioner.

Nripendra Narayan, M.B., B.S. (Patna), Civil Assistant Surgeon, Bihar.

Gopal Ranganath Patwardhan, L.C.P. & S. (Bom.), Private Practitioner.

U. Ohn Pe, L.M.F., L.H. (Burma), Assistant Malariologist, Government of Burma.

Karan Pershad, M.B., B.S. (Hyd.), Assistant Civil Surgeon, Hyderabad State.

Vasant Wasudeo Puraik, B.Sc., M.B. (Cal.), Private Practitioner.

T. S. Srinivasa, B.M. & S. (Madras), Assistant District Health Officer, Tanjore.

Nirmal Chandra Roy, M.B. (Cal.), Private Practitioner.

Jagdish Chander Sarin, M.B., B.S. (Punjab), Bacteriologist, Public Health Laboratory, Jaipur State.

Joy Gopal Sarma, M.B. (Cal.), Private Practitioner.

Nani Gopal Sen, L.M.F. (Dacca), R.M.O., Central Hospital, Duars Tea Co., Ltd.

Autar Singh Sethi, L.M.S., Private Practitioner.

Ranjeet Bhagwan Singh, M.B., B.S. (E. Punjab), Private Practitioner.

Jugal Kishore Prasad Sinha, M.B., B.S. (Patna), Civil Assistant Surgeon, Government of Bihar.

Rahindra Nath Sur, M.B. (Cal.), Private Practitioner.

The Indian Medical Gazette Fifty Years Ago

THE ANNUAL MEETING OF THE BRITISH MEDICAL ASSOCIATION

(From the *Indian Medical Gazette*, April 1900,
Vol. 35, p. 143)

THE 'preliminary programme' of the Annual Meeting of the British Medical Association which is to be held at Ipswich on Tuesday, Wednesday, Thursday and Friday, July 31st to August 3rd, inclusive, has been issued. It includes a list of the office-bearers of the Association and of the thirteen sections, the names of those who are to deliver addresses on medicine, surgery and obstetrics, and a general time-table of the proceedings of the meeting. It remains now for the officers of the several sections to arrange for the business which will be transacted in each. This will, as usual, consist of discussions on previously selected

subjects and the reading of papers. The subjects which have been adopted for discussion in the tropical diseases section, which will naturally elaim the special attention of medical men praetising in the tropics, are :—

1st. Quinine and its action and modes of employment in malaria.

2nd. Ancylostomiasis.

3rd. The ætiological and pathological relationships of yaws.

On each of these topics interesting and important questions arise and valuable information ought to be forthcoming.

The prophylactic use of quinine

One of the main points concerning the use of quinine in malaria is its preventive function. This presents a twofold aspect accepting its germicidal power as regards the plasmodia of malaria and conceding the point as regards their being a contagium vivum capable of multiplication in man and conveyance from man to man by certain agencies; the destruction of these parasites in the blood must necessarily exercise a prohibitive influence of a radical kind, and this point has recently been emphasized by Bignami in a paper published in the *Lancet*. But does the drug also hinder development and multiplication of the germs in the blood to such an extent as to avert or abort pathological consequences in persons inoculated or infected by these organisms? Or, generally, does it counteract or inhibit the action of the malarious noxa whatever its nature? On this phase of the question it is very desirable that the results of the trials which have been made in Indian gaols for some time past should be intelligently studied and summarized. A mere comparison of one year with another or one community with another will not suffice. A comparison of two sections of the same community living in all other respects under identical conditions is necessary. In other words we must have controls. Recorded experiments made under such circumstances would be greatly prized.

Ancylostomiasis

The principal points relating to this form of anæmia and cachexia arising from infection by the ancylostomum duodenale are the relation of the constitutional depravity to the number of parasites infesting and the health and condition of the host infested, and the relation of the cachexy to other tropical cachexies such as chronic paludism, tropical or scorbutic anæmia and beri-beri. The experience gained by a study of the condition in Assam and Ceylon on the one hand, and in Egypt and Brazil on the other, ought to establish contrasts and checks which should place the true causation and gravity of the complaint on a more satisfactory basis.

The ætiology and pathology of yaws

Is this disease an exanthem or an infective granuloma? Is it a secondary manifestation of syphilis or a disease *sui generis*? Are these mutually protective? Is yaws communicable and self-protective? What is the precise nature of 'paranghi' disease of Ceylon? What of the veruga of the elevated valleys of the Andes? What affinities do these possess with frambæsia if any? These are some of the questions on which more light is wanted and a surer decision required. The discussion will give opportunity for men hailing from different and widely-separated places to contribute the results of their observation and experience. It is this bringing together of many men from many parts with many facts and many views which imparts to these meetings their special interest and use, and I hope that the present meeting of the tropical diseases section will equal, if not surpass, its two predecessors in these respects.

The mosquito theory

The Liverpool School of Tropical Diseases has issued a pamphlet of 'instructions for the prevention of malarial fever' based on a thorough acceptance of Laveran's plasmodia as the parasitic cause of malarial diseases and of certain species of mosquito as the agents of transference of these from the diseased to the healthy organism. On this basis the pamphlet is both logical and lucid, and its precepts admirable. About the same time that I received this pamphlet your January number came to hand in which both the props on which these views and instructions rest are roughly and somewhat dogmatically assailed. Nothing but benefit can be derived from criticism, especially when founded on research, and the principle of *audi alteram partem* is unquestionably sound; but it strikes me that the element of detraction and contentiousness which is too apparent in the article to which I refer ought to be vigorously eliminated as its existence or apparent existence serves largely to depreciate the value of the work.

Sir Joseph Fayrer's reminiscences

It has been known for some time that Sir Joseph Fayrer has been engaged in compiling the annals of his eventful life and brilliant and useful career. The announcement is now made that this work will shortly be published. It will be read with avidity, and as its distinguished author has been in the habit of making copious notes of all the important incidents of his service, the book will be a rare treat for members of the Indian Medical Service who have learned to look upon him as a guiding star and champion. Loyalty to his own service has ever been one of the most influential motives of Sir Joseph's life, and I doubt not that this has awakened a feeling of grateful recognition in the service at large.

The suppression of rabies in Great Britain

It is reported that for the present at any rate rabies is extinct in Great Britain, and in consequence the muzzling order has been cancelled with a few unimportant exceptions. This satisfactory result has been obtained by measures directed against rabid dogs obtaining entrance into the kingdom, and preventing dogs which becoming rabid in the kingdom from communicating the disease to man or beast by means of the muzzle. The result is a signal and successful example of the utility of operating against diseases common to man and the lower animals by taking steps to thwart the communication of these by the latter to the former. The campaign against mosquitoes and rats derives justification from this experience. Of course, the steps appropriate in different instances must depend upon the differing circumstances of the case; but the principle is an important one, and its execution adds materially to our preventive resources against disease. It is curious to find the property of infectiveness used in warfare for the purpose of disabling an antagonist. The Boers at Modder River are said to be allowing horses affected with 'pink eye' to stray into the British camp apparently with the object of crippling our cavalry. This dodge is in keeping with the reputed use of cyanide of potassium for the purpose of poisoning water-courses, a barbarous and murderous expedient which our enemies are said to adopt when the occasion offers.

K. McL.

8th February, 1900.

Current Topics, Etc.

Aureomycin in Infections of the Urinary Tract

By J. R. FRANKLIN

(From the *Ohio State Medical Journal*, Vol. 45, May 1949, p. 460, as abstracted in the *International Medical Digest*, Vol. 55, September 1949, p. 152)

The use of aureomycin in the treatment of 10 patients with chronic and resistant bacillary infections of the urinary tract is presented. 'In the majority of these cases the infecting organism was of the *E. coli* group and several had a mixed infection of both *E. coli* and staphylococcus.'

'Aureomycin appears effective against urinary tract infections due to *E. coli* where other measures have failed. If the focus of infection is associated with a chronic pyelitis, chronic prostatitis or other focal abscess, the drug cannot be expected to sterilize this focus. However, in such cases relief of bladder symptoms and the return of a "clear" urine can be achieved pending the application of more specific measures. The drug may be given for a few days before and for a week following prostatectomy to control the inevitable bladder infection. The resistant infections

seen in the "cowl" bladder of neurosyphilis or following combined resections of the lower colon are amenable to treatment with aureomycin. In one such case treated successfully the urine was so "milky" with pus that difficulty was experienced in catheter drainage. Culture of the urine in a dilution of 1 to 1 million grew out 400 colonies of *E. coli* on the agar plate. Aureomycin in a dosage of 1.5 gm. daily produced a clear urine, sterile to culture, in four days. Symptomatic relief of the patient was equally dramatic. Several female patients seen in office practice with chronic and recurrent cystitis and trigonitis were successfully treated. In one of these, repeated catheterized urine cultures failed to demonstrate any infecting organism, yet symptomatic relief was obtained promptly and 'pus cells disappeared from the urinary sediment.'

Encouraging results were obtained in all 10 cases reported.

'The simplicity in administration of aureomycin is appealing. No gastrointestinal complaints due to the use of the drug were encountered. One female patient developed a crural dermatitis spreading to the inner aspect of the thighs that was thought to represent a sensitization reaction. This dermatitis subsided promptly on withdrawal of the medication. Frequently a peculiar yellowish green opalescence was noted in the voided urine and was considered to be due to pigment derived from the drug. This colour effect in some cases persisted for a considerable time after the medication was stopped.'

The cases in this study were selected because the writer wished to note the response to the drug in a variety of urinary tract infections where *E. coli* was the predominating organism. It is in the control of this type of infection that he has previously experienced the greatest difficulty. 'Reinvasion on the urinary tract by the infection may occur following the withdrawal of the drug if adequate drainage is lacking or if the original focus of infection remains. In such an event retreatment may be necessary. There is evidence that some of these infections may be kept under control by more prolonged administration of the drug in reduced dosage.'

Subdeltoid Bursitis

By P. E. WYLIE

(Abstracted from the *Military Surgeon*, Vol. 105, September 1949, p. 237)

SUBDELTOID bursitis is an excruciatingly painful peri-articular affection of the shoulder. It is sometimes referred to as *periarthritis* or *para-arthritis* and in the chronic stage is known as frozen shoulder. It comprises 85-90 per cent of all painful shoulders excluding acute sprains, fractures and dislocations. It has no respect for sex, colour or adult age. The aetiology of this disease is not known.

The chief symptom of acute bursitis is severe, sharp, debilitating pain. It is knife-like in character and usually remains fairly well localized to the tip of the shoulder. In a few patients, a less severe pain radiates down the arm and into the hand. Limitation of motion is a constant feature. All attempted voluntary motion is in the scapula on the body instead of the shoulder joint. The patient usually comes to the office with his arm in a sling and is very careful to completely protect it. The pain is so severe that it prevents sleep and requires rather large doses of morphine for partial relief.

The attacks are sudden in onset. The patient is usually awakened from sleep by the constant persistent pain and is at a loss to know what has happened. Many, however, refer to some minor injury that they experienced a day or so preceding the onset. This trauma is usually in the form of throwing a ball,

reaching above the head for some object, or sleeping in a draft.

These are the symptoms of acute bursitis and if not treated will probably last for a week or ten days. Then, they gradually subside to leave a tender, moderately painful shoulder. Motion remains impaired to at least 75 per cent.

Physical examination only confirms the symptoms as related by the patient. There is finger-point tenderness at the tip of the shoulder, limitation of both active and passive motion, and a general apprehensiveness. Motion is more freely carried out in the subacute and chronic cases, but the patient cannot scratch his back or empty his hip pocket. Abduction and internal rotation are the most difficult motions. The shoulder looks normal to inspection as there is no swelling or redness.

X-ray examination reveals calcific deposits in about 50 per cent of cases examined. Exact location of the deposits cannot be determined, but they usually lie in the reign of the supraspinatus tendon. Often, acute cases show nothing unusual. Chronic cases may show calcification and if so, it is more dense and bone-like than in the acute ones. They also show bone changes of disuse, i.e. osteoporosis. Occasionally, on routine x-ray examination of the shoulder periarticular calcifications will be seen which are symptomatic. So, visualization of the deposits does not necessarily mean that an active inflammatory process is present. Calcifications in the bursæ or tendons can be differentiated from fractures by their homogeneous character and lack of a corresponding defect in the humerus. X-ray exposures should be made in the A-P view in both external and internal rotation. If only one film is made, calcium deposits may be hidden behind the head of the humerus.

There have been many forms of treatment advocated for acute bursitis. Sufficient amounts of opiates and barbiturates to relieve the patient most certainly should be prescribed. Short-wave diathermy has been tried and discarded as aggravating the condition. Physiotherapy, in a combination of massage, gentle passive motion, and whirlpool baths, has proved to be efficacious in a few cases. Injection of novocaine with aspiration of the calcific milk is advocated by some. Surgical removal of calcific deposits has been resorted to; however, this form of treatment seems to be a little on the radical side.

The most generally accepted and successful method of treatment to date has been x-ray therapy. The beam of rays is directed to the top of the shoulder and a dose is given twice a week for two weeks. One series usually will completely relieve the acute cases. When the lesion has existed for more than a month or is in the subacute stage, the first series of treatment is extended to four weeks. If at the end of this period the patient is not better, this form of treatment is discontinued. If he is better and not well, treatments may be repeated after a lapse of six to eight weeks. Chronic cases are selected for treatment according to their severity. Frozen shoulders are not benefited. Lesions of less severity may show partial relief. The amount, interval and duration of treatment must be dictated by the condition of the patient.

Somatic Movements of the Prematurely Born Fœtus—Film Demonstration

By I. MACKENZIE

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. 42, November 1949, p. 877)

THE infant born at the end of five months had still about another five months to live before myelination began in the pyramidal tracts and a corresponding delay was noted in the ontogenesis of the corpora

striata in the higher vertebrates. Each of these nuclei comprised two distinct bodies which differed fundamentally both in structure and in function. The pallidum or paleostriatum was more medially situated and appeared in the lower vertebrates as a motor centre in relation to the vegetative functions of the hypothalamus. The other portion, the neostriatum, including the putamen and caudate, appeared later in relation to the evolution of the neopallium or cerebral mantle, and had to do with the wider range and variety of movement which that expansion implied. The course of myelination in the corpora striata in the human subject reflected the intrinsic sequence of events in the evolution of these bodies. Already in the sixth month of foetal life there was evidence of myelination in the pallidum and at full-term birth the fibres which connected the pallidum with the thalamus and hypothalamus were for the most part myelinated, whereas those which entered the pallidum from the putamen or neostriatum were still without myelin. It was thus reasonable to assume that the infant prematurely born at five months or six months or later, was a 'thalamo-pallidal creature' and that the somatic movements which it executes such as breathing, chewing, swallowing and excretion, as well as other incidental movements like grasping, kicking, movements of the eyes, of the head and neck, and movements of expression may all be ascribed to the early development of the neural apparatus in the more caudal part of the brain-stem and spinal cord.

The prematurely born foetus was suddenly subjected to the tests of an abnormal environment. Deprived not only of maternal nutrition but of the security and warmth of the amniotic medium it had to fend for itself. To survive it must breathe, swallow, digest and excrete and the internal milieu must be such as to provide for the maintenance of an equable temperature. Survival depended on the fact that the vegetative system took precedence in the process of development; and its somatic components were the first to exhibit the regular and orderly activity of striated musculature. The muscles of breathing, sucking, swallowing, and excretion exercised a physiological function in the sense that they served an organic purpose and contributed to survival, whereas the movements of the limbs, of the head and of the eyes were irregular and purposeless so far as serving the immediate requirements of the organism was concerned. This, of course, obtained also in the case of the foetus born at full term but it was possible to discern in the prematurely born foetus from five or six months onwards special activities and reactions which were more or less regular way in the course of development and may thus be taken as an expression of the progressive construction of the central nervous system. Outstanding among these were activities and reactions described by the experimental physiologists such as 'grasping', 'pedal rhythm' and 'startle reflex' of Magnus and de Kleijn. These were in themselves phenomena of significance inasmuch as they demonstrated the validity of the conclusions based on the experimental methods devised to demonstrate the function of the nervous mechanism by operative interference with its component parts.

The most dramatic feature of survival from early premature birth was the persistence with which the organism preserved its identity and the consistency with which it pursued its course towards maturity, and all this in spite of abnormal environment. The process of construction and the emergence of function proceeded according to time-table. The course of events would seem to be directed by an 'inner-drive', a destiny in the design of nature.

No less striking was the efficiency with which the vegetative system operated on premature delivery, even at five or six months. This derived, no doubt, from phylogenetic inheritance which secures, at an early date, a complete development of the tegmental and spinal structures essential for respiration, alimentation and excretion. Breathing and swallowing are

subservied by a common mechanism in the substantia reticularis so differentiated that from the start they operate in harmony and in mutual exclusion. There was no disorder such as coughing or sneezing or hic-cough or vomiting which mark the derangement of these mutually integrated though independent activities. Whether, and if so in what sense, the 'pedal rhythm' and 'neck reflexes' were indicative of an 'inner-drive' is a matter for further investigation. In any event the rhythmic movement of the lower limb at five months did suggest an intrinsic rhythm comparable with that described by Graham Brown, whose experiments led him to conclude that there is a 'rhythmic centre' in the lumbo-sacral enlargement comparable with the 'respiratory centre' in the medulla. It did not in the least detract from the value and importance of the Sherrington School in the elucidation of the structure and function of the nervous system from the point of view of reflex activity to suggest that there were other factors of an inherent character such as 'intrinsic rhythm' which contributed to the activity of the system as a whole.

A Simple New Stain for Intestinal Protozoa

By M. I. E. KORDY

(From the *Journal of the Royal Egyptian Medical Association*, Vol. 32, May 1949, p. 426)

THE author has discovered a new stain for nuclear and differential staining of intestinal protozoa. This stain is the infusion obtained by boiling the brownish outer skin of the Egyptian onion (*Allium cepa*). The infusion contains quercitrin which is one of the most widely distributed natural pigments. It occurs in many plants such as horse-chestnut, vine leaves, hops, tea, and dye's oak (*Quercus tinctoria*). Its chemical composition is $C_{21}H_{30}O_{11}$ (yellow needles, m.p. 182-185°C.). Its chief colouring component is quercetin, which is a pentahydroxyflavone, $C_{15}H_{10}O_7$ (3, 5, 7, 3', 4'-pentahydroxyflavone, yellow crystals, m.p. 316-317°C.).

Quercitrin is a 3-rhamnose glycoside. The infusion can be used as a stain immediately after its preparation. Time or additional material are not required for ripening as in the case of hematoxylin stain. Neither mordant nor differentiation were needed.

Preparation of the infusion.—As much as possible of the brownish skin of onions is placed in a vessel and tap water is added to just cover it. The vessel with its contents is placed on the fire and the water is kept boiling until a deep brownish colour is observed. This brownish infusion is used as the solution for staining of intestinal protozoa. When the infusion is stored, some sediment occurs, but this does not interfere with staining.

Method of staining.—Fix in Schaudinn's fluid (saturated solution of mercuric chloride 100 parts, absolute alcohol 50 parts and glacial acetic acid 7.5 parts) as follows:—

1. Place fixative in petri-dish.
2. Holding cover slip in the left hand, between thumb and index, make a thin smear of infected stool with a match or a platinum loop and drop the slip face downwards into the fixative (later turn it face upwards and continue further manipulations in this position).
3. Fix for about 25 minutes.
4. Transfer to petri-dish containing 70 per cent alcohol and a little iodine (Weigert-Lugol's iodine) for 30-60 minutes.
5. Transfer to pure 70 per cent alcohol (2 changes). In this the preparation can be kept for one hour or an indefinite period of time before staining. If the slip

is to be stored, it should be placed in a glass cylinder and covered with cotton-wool to prevent breakage.

Staining:—

1. Transfer the slip from 70 per cent alcohol to the dye solution which is diluted with 70 per cent alcohol (staining solution 4 parts, and alcohol 1 part) for about 2 hours at 37°C. If left overnight at 37°C., better results may be obtained. Undiluted stain may also be used. Staining also occurs at room temperature.
2. Transfer slip to tap water and leave in running water (or several changes of same) for about 4 minutes.
3. Dehydrate successively in 70, 90 and 100 per cent alcohol (about 10 minutes in each).
4. Clear in xylol for about 10 minutes.
5. Mount in Canada-balsam.

Caution.—Throughout the whole process of fixation and staining, from the moment the smear is made until it is mounted, the preparation should never be allowed to dry, otherwise it will be ruined.

This infusion of onion skin produces a stain which shows great selectivity and contrast between the nucleus and cytoplasm and between chromatin and the rest of the nucleoplasm. In selectivity and contrast as nuclear stain it gave results equal if not superior to the well-known hematoxylin solutions.

SUMMARY

The infusion of the brownish outer skin of the Egyptian onion (*Allium cepa*) was found to possess an excellent tinctorial power for the staining of intestinal protozoa. Neither mordant nor differentiation was needed. The tinctorial power of onion skin infusion is due to the natural pigment quercitrin.

Folic Acid and Neurologic Changes in Pernicious Anæmia

(From the *Canadian Medical Association Journal*, Vol. 61, August 1949, p. 172)

CONSIDERABLE attention has been given to the status of folic acid in the treatment of pernicious anæmia (*Nutrition Reviews*, 5, 208, 274, 1947; 6, 90, 114, 245, 291, 1948). It has been observed repeatedly that not only may folic acid fail to halt progression of the neurologic changes associated with the disease, but actually may increase them.

Further evidence for the failure of folic acid to halt neurologic disturbances is given by S. D. Jacobson, L. Berman, A. R. Axelrod, and E. C. Vonder Heide (*J. Amer. Med. Assoc.*, 137, 825, 1948). Two patients with pernicious anæmia in relapse were treated with varying but rather large amounts of folic acid (10 to 65 mg. daily). Both had evidence of combined systems disease before therapy. A maximum reticulocyte response occurred at the expected time following folic acid therapy and the hæmoglobin and red blood cell counts began to rise. Approximately sixty and one hundred and twenty days after folic acid therapy was begun and while 10 mg. of the material were being administered daily orally, neurologic symptoms and signs reappeared, progressed rapidly, and became severe. Both patients were then given liver extract instead of folic acid, but in only one is its effect upon the neurologic lesions given, in this case remission.

The authors suggest that further clinical trials be made with larger amounts of folic acid to observe whether a progression of the neurologic changes can in this way be prevented. The evidence indicates that this would not be a safe or effective procedure. Since liver extract is at least known to halt progression of neurologic disease and often to effect a complete remission, this material would still seem to be the indicated material for the treatment of pernicious

anæmia. The discovery of vitamin B₁₂ (*Nutrition Reviews*, 6, 245, 291, 1948) and its dramatic clinical effect in the treatment of pernicious anæmia, both for the blood and neurologic disturbances, may in time supplant the use of liver as the therapeutic agent of choice in pernicious anæmia.—*Nutrition Reviews*, February 1949.

The Cytological Diagnosis of Malignant Cells in Various Body Fluids

By H. E. TAYLOR

and

W. J. THOMPSON

(Abstracted from the *Canadian Medical Association Journal*, Vol. 61, October 1949, p. 413)

BECAUSE of the interest in cytological methods for the diagnosis of malignancy, it was felt that it might be of interest to review the results obtained at Shaughnessy Hospital in order to ascertain the accuracy of the methods in use and to determine if possible the usefulness of such procedures.

For the purpose of analysis the authors have reviewed all the cases in whom pleural fluids, ascitic fluids, sputa or gastric washings have been examined for the presence of neoplastic cells. This comprised a total of 164 specimens from 103 patients during the interval between January 1946 and June 1948.

The examination of pleural fluid, ascitic fluid, sputum and gastric washings has proved of diagnostic value in the series of 164 specimens from 103 patients reviewed. In all, positive reports were made in 34.9 per cent of cases. The method was accurate in 92.8 per cent of cases, there being 4 false positive reports in the entire series. These comprised 7.2 per cent of fluids examined from patients eventually shown to have no malignant neoplastic lesion. These results compare favourably with other reported series.

The false positives were confined to pleural fluids. It is emphasized that the utmost conservatism should be maintained in interpreting neoplastic cells in transudates or exudates since endothelial cells proliferating in such a 'culture' medium may assume very bizarre shapes and forms.

The authors recommend cell block preparation as described by Hunter and Richardson in preference to the smear technique. In their hands, they have found the former method to give higher positive results.

The usefulness of this procedure when viewed from the treatment aspect proved disappointing, since the finding of neoplastic cells indicates a very grave prognosis. The average duration of life from the first positive report was only 4 months.

Healed Subacute Bacterial Endocarditis: A New Entity

By S. R. KAPLAN *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 10th September, 1949, p. 114)

WITH the advent of more successful therapy, a cure of the active infection has been achieved in a significant number of cases, and greater attention must now be anticipated as the methods of treatment progress. In the entity of healed subacute bacterial endocarditis, increasing examples of a new complication are appearing. These patients represent a previously unanticipated course of events. With adequate therapy, complete arrest of the infection has resulted, but

damage sustained by the heart before the disease was brought under control has contributed to the deterioration of the patient through the development of congestive heart failure.

This report concerns the subsequent course of a group of 18 patients whose subacute bacterial endocarditis was treated and whose active infection had been cured. Michael Rees Hospital during the years 1944-1947. The minimum follow-up period is twenty-five months, the maximum sixty-one months.

Six patients (one-third) have shown progressive cardiac disability since the onset of the endocarditis. In three the disability was so severe as to lead to death from congestive heart failure eight, nine and thirty-nine months, respectively, after cure of the infection. The single common factor in all six of these patients is dynamically significant insufficiency of the aortic valve, which led to strain of the heart.

Twelve patients have shown no progression of their cardiac status in spite of the existence of healed subacute bacterial endocarditis. In none of these is there dynamic aortic insufficiency, although acoustically it was noted in three instances.

No correlation can be found between progressive cardiac disability following cure of the infection and age, sex, duration of illness prior to treatment, length of hospital stay or total penicillin dosage.

The significance of penicillin in the development of progressive heart disease is discussed.

Refractory Amoebic Abscess of the Liver treated with Chloroquine

By J. EMMETT

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 22)

A CASE of amoebic abscess of the liver was refractory to emetine therapy but was successfully treated by chloroquine diphosphate.

Advances in microbiologic technique have made possible more rational treatment of a secondary wound invader.

Reviews

TEXTBOOK OF OPHTHALMOLOGY.—By Sir W. Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Ph.D., M.D., Ch.B., F.R.C.S., etc. Volume IV. *The Neurology of Vision, Motor and Optical Anomalies.* 1949. Henry Kimpton Ltd., London. Pp. xxiv from 3473 to 4627. Illustrated. Price, £3-10-0

It has been a pleasure to go through the fourth volume of the Textbook of Ophthalmology by Sir William Stewart Duke-Elder, which has made its belated appearance in conformity with the first 3 volumes.

As usual with the other volumes, this one deals exhaustively with neurology of vision, motor and other optical abnormalities in the course of 1200 pages. The book begins with Anatomy, Physiology and Pathology of the visual pathways and ends in the last chapter of 100 pages with details of clinical optical appliances.

A practical physiologist of repute, Sir William Stewart Duke-Elder has left little unsaid about dis-

orders of visual centres, in dealing with neurology of vision. The nomenclature of different types of aphasia is at once illuminating and useful.

The exhaustive dealing on the subject of motor anomalies is all that any student of ophthalmology would desire.

There are 3 sections in the book, namely, (1) Neurology of vision, (2) Motor anomalies of the eye and (3) Optical anomalies of the eye. Each of these sections begins with historical consideration, proceeds with general considerations, aetiological factors, pathogenesis, signs and symptoms, and ends with fairly exhaustive discussions on treatment. The chapter on anomaly of pupillary pathways provides all the information available on this controversial subject.

The last chapter on clinical and optical appliances require special notice. Few students of ophthalmology are fully acquainted with the process of manufacture of spectacle lenses and details of spectacle optics. This chapter lays open these subjects to the reader.

Numerous references in brackets appear throughout the pages. Perhaps exhaustive bibliography at the end of the chapter should have sufficed.

The illustrations and get-up of the book are excellent.

S. C. D.

SEX AND ITS MYSTERIES.—By G. R. Scott, F.Z.S., F.Ph.S. (Eng.). 1948. Torchstream Books, 50, Alexandra Road, London, S.W.19. Pp. 214. Price, 12s. 6d.

SINCE a decade or two it has been realized that the knowledge of sex and sex-science should not be kept a secret but imparted to every young man and woman in their adolescence. The knowledge of sex anatomy and physiology is as valuable and important to an individual as the knowledge of the parts of his body. Locking up the atom-secret of the sex knowledge and its mysteries is considered not only useless but actually harmful, particularly at the present stage of human intelligence and social development.

The present book is in the eighth series of the library on the modern science. It was first published in 1929. The present edition is divided into 22 chapters along with a glossary of the biological and the medical terms used in the text. This glossary was considered necessary since without its aid the text may not be easily understood by a lay reader. The book is written in a very simple language and can be read like a novel. The chapters on the description of the male and the female sex organs, the story of the development and the growth of the embryo, pregnancy and the child birth are very fascinating and full of information. These early chapters form a basis for the layman to follow up the succeeding sections. There are interesting revelations in the chapters on prostitution, birth control, artificial insemination, the prevention of venereal diseases, etc.

J. S. C.

FORENSIC MEDICINE: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS.—By Sir Sydney Smith, C.B.E., M.D. (Edn.), F.R.C.P. (Edn.), D.P.H., and Frederick Smith Fiddes, O.B.E., M.D. Ninth Edition. 1949. J. and A. Churchill Limited, London. Pp. xii plus 659 with 173 illustrations. Price, 30s.

This well-known book has appeared in its ninth edition under a joint authorship after a thorough revision of the text.

New items included are: (1) part played by adenosine triphosphate (ATP) in the contraction of muscles and in rigor mortis. The substance decom-

poses and disappears after death, resulting in the conversion of actomyosin of the living muscle into a stiff gel of the dead muscle. (2) Rh Factor. The medicolegal significance of this new blood character is discussed. As the various antisera become more generally available and the basic hypotheses become more firmly established, the tests are bound to become more widely applicable and legally acceptable. (3) BAL. This therapeutic agent is useful in poisoning by (i) arsenic, organic or inorganic, acute or chronic, (ii) mercury, (iii) gold and (iv) possibly all other metals. (4) Addition of certain drugs—pethidine, desomorphine, preparation of Indian hemp, amiodone and metopon to the list of the Dangerous Drugs Act.

Other items of special interest in the book are: (1) Diminished responsibility. This midway position between perfect immunity from and full responsibility for crime, is more in accord with the medical opinion than with the McNaughten Rules. (2) Forensic medicine in the East. A remarkable case of suicide by an apparently normal Egyptian attendant at the court of appeal is described. The man ripped open his abdomen with a razor and cut off a portion of the omentum, large intestine and stomach, and then cut off his penis and testes. He spoke rationally to the senior author 10 minutes afterwards and lived for half an hour. Ordinarily and elsewhere such a brutal treatment of the body would go against a presumption of suicide.

One point needs clarification: The book states that an expert can give an opinion on broken spermatozoa. The senior author in another book insists on *at least one unbroken spermatozoon* for a positive answer.

The recent National Health Service has not been included. National Insurance (Industrial Injuries) Act which supersedes the Workmen's Compensation Acts has been included. War gases have been excluded. The get-up is good and price reasonable.

An excellent publication.

S. D. S. G.

BOOKS RECEIVED

1. The Deaf in India. Official Organ of the Convention of the Teachers of the Deaf in India, 50, Bondel Road, Ballygunj, Calcutta 19. Vol. II, No. 1, April 1950. Editor A. C. Sen and Associate Editor B. K. Chakravarti.

2. Compost Bulletin. Vol. II, No. 4, December 1949. Issued by the Compost Development Officer, Ministry of Agriculture, Government of India, New Delhi.

3. Preparation of Compost Manure from Farm, Village and Town Wastes. By Dr. C. N. Acharya, Ministry of Agriculture, Government of India, New Delhi.

4. The United Provinces Veterinary Magazine. Chief Editor H. P. Kapoor, M.Sc., A.B.V.C., c/o U. P. College of Veterinary Science and Animal Husbandry, Mathura.

5. Proceedings of the Society for the Study of Industrial Medicine. Vol. 11, No. 1, March 1950. Editor Lieut.-Colonel Najib Khan. The Society for the Study of Industrial Medicine, Jamshedpur, India.

6. The Madras Veterinary College Annual, 1949-50. Editor C. N. Ganapathy, B.A. Associate Editor S. V. Sunder Singh. Vol. VIII, January 1950. Inland Rs. 2. Foreign 2s. 8d. Papa Press, Madras 2.

7. Transactions of the National Institute of Sciences of India. Vol. III, No. 4, pp. 159-209 (6 Plates and 23 Text-figures). A Contribution to the Morphology and Anatomy of the Cyclanthaceae. By K. R. Surange, M.Sc., Research Fellow, University of Lucknow, National Institute of Sciences of India, Delhi. Price Rs. 9-0-0.

S. Compost Bulletin. Vol. II, No. 2, June 1949. Issued by the Compost Development Officer, Ministry of Agriculture, Government of India, New Delhi. Printed in India by the Manager, Government of India Press, Simla, 1949.

Abstracts from Reports

ANNUAL REPORT ON THE HEALTH OF THE ARMY IN INDIA FOR THE YEAR 1947. PUBLICATION NO. 29393/AG/ORG/IASO/PERS (MED.), A.G. BRANCH. PRINTED BY THE GOVERNMENT OF INDIA PRESS, NEW DELHI, FOR THE MINISTRY OF DEFENCE DEPARTMENT, GOVERNMENT OF INDIA, NEW DELHI

THE present report, in addition to giving a general perspective of the health of the Defence Forces in India, bears a special interest since India in the year under review passed through extraordinary and important political changes. The partition of the country and subsequent division of the Indian forces, the communal riots and civic commotions are occurrences not known in the history of the country. Another interesting feature is that a review on the reports is being written when the country is witnessing another exodus of population and probably another upheaval* even greater than that in the year 1947. During such upheavals the Defence Forces of the country have to bear the brunt in the form of defence of the country, care of the warring masses and the salvage work for the helpless refugees who are enduring terrible physical and mental strain. In the year 1947, the Indian troops were called up to defend and protect the State of Jammu and Kashmir, when the hostiles from Pakistan and the tribal areas raided it. The troops exhibited splendid strength and perseverance in the face of severe trials. The difficulties of temperature and altitude were great. Probably a modern army has never yet fought under such conditions.

(1) The general sick state of the officers of the Indian army was 350.76 per thousand as against 437.1 in the year 1946. The sick state of the V.C.O.s. and the other ranks was also far more satisfactory than in the preceding year. (2) The malarial infection: The admission rate was 33.62 per thousand and this was the lowest for the last 15 years. (3) The dysentery and the diarrhoea admission rate rose slightly to 36.58 per thousand against 23.4 in 1946 but on the whole this infection was under control and was on the decline after the war. (4) The venereal infection, which has been on the rise since 1939 and reached its peak of 50.55 per thousand in 1943, was now on the decline and was at 45.5.

The sections on organization, food and nutrition and on the clinical pathological service are also interesting. The training in the pathology and the research work and general training in the I. A. B. T. College, Poona, is very intense and of high order both for the officers and the assistants.

The efficiency of the army as a whole has considerably improved and suffered no loss since the passing of the British limb of the forces. Papers on the following subjects were published: Anæmia investigation, marasmus and sprue; arsenical encephalopathy in the Indian troops; Lamallary atrophy of the Purkinje's cells following heat hyperpyrexia; and the salmonella infection and the diphasic variations of the salmonella paratyphoid-A.

J. S. C.

* Written before the 'Delhi talks'.—EDITOR, I.M.G.

Any Questions

PRIMARY AND RELAPSING MALARIA

SIR,—Will you please be kind enough to let me know through the columns of your journal the methods of differentiating a particular attack of malaria—either clinically or by laboratory methods—as a relapse of previous infection or a fresh infection, i.e. reinfection.

Yours faithfully,

C. M. PATWA, M.B., B.S. (Bom.).

NASIK CITY.

It is often difficult or impossible to make a distinction between primary and relapsing cases of malaria. Generally it is true that relapses are usually milder (clinically) and that the peripheral blood films may show the sexual forms (gametocytes) more promptly than in a primary attack, yet after a suppressive antimalarial therapy, a delayed primary attack frequently resembles a relapse in these points. In areas or seasons devoid of mosquito malaria vectors or in individuals exposed for the first time to malaria, it is usually possible to differentiate between primary attacks and relapses, but when infection is an ever-present possibility, it is very difficult (practically impossible) to distinguish between them. One must use, in such circumstances, professional judgment—as there are no helpful clinical or laboratory criteria.—S. S.]

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CONTENTS

Page

ORIGINAL ARTICLES

Gonococcal Arthritis. By S. L. Malhotra, M.R.C.P. (Lond.), D.C.H. (Eng.) .. 187

Disseminated Lupus Erythematosus. By N. R. Konar, M.D. (Cal.), M.R.C.P. (Lond.), and D. Banerjee, M.B., M.R.C.P. (Lond. and Edin.) .. 188

Post-necrotic Scarring of the Liver in a Child and its Possible Relationship to Rh Factor. By B. P. Tribedi, M.B. (Cal.), D.B. (Lond.), F.N.I., and N. K. Chanda, M.B. (Cal.) .. 192

Congenital Atonic Diplegia. By J. N. Berry, M.D., M.R.C.P., D.C.H. .. 195

'Myoidema' and 'Myotatic Irritability'. By P. L. Deshmukh, M.D. (Bom.), D.T.M. & H. (Lond.), F.C.P.S. (Bom.) 197

Experience with Floccillin '96'. By M. Dutt, M.B., Major, I.A.M.C., and P. N. Bardhan, Lieutenant-Colonel, I.A.M.C. .. 199

Chemotherapy of Cholera with a New Sulphone Compound. By M. Abdulla, L.C.P.S., L.M.S., and D. K. Rohini, L.M.P., L.G.O. .. 202

Aureomycin in the Treatment of Typhoid, Typhus, Cystitis and Pertussis. By K. V. Krishnan, R. N. Chaudhuri, H. Chakravarti and M. N. Rai Chaudhuri 202

A MIRROR OF HOSPITAL PRACTICE

Mediastinal Lymphosarcoma in a Child. A case report. By A. B. Mukerjee, M.D., M.R.C.P. .. 206

A Case of Acute Nephritis treated with an Antihistamine Drug. By A. Samad, M.B., and S. C. Kapoor, M.D. (Luck.) 208

EDITORIAL

Geriatric Medicine .. 209

MEDICAL NEWS

LEPROSY TRAINING COURSE .. 212

SOAPLESS 'SOAP' TO DISSOLVE THE INSOLUBLE. 'RADIOSONDE' RECORDS TEMPERATURE AND HUMIDITY OF UPPER AIR. SCIENTIFIC RESEARCH IN MANY FIELDS .. 212

Page

'JOURNAL OF SCIENTIFIC AND INDUSTRIAL RESEARCH'. ROCK SALT DEPOSITS OF MANDI .. 213

PUBLIC HEALTH SECTION

The Use of Potassium Permanganate in the Disinfection of Water. By Radhakrishna Banerjee, M.B., B.S., D.T.M., D.P.H. .. 214

FIFTY YEARS AGO

THE TEACHING OF HYGIENE IN INDIAN UNIVERSITIES (*Indian Medical Gazette*, May 1900, Vol. 35, p. 181) .. 219

CURRENT TOPICS, ETC.

BEEL, J. A., PITTMAN, MARGARET & OLSON, B. J. PERTUSSIS AND AUREOMYCIN. PUB. HEALTH REP., WASH., 1949, MAY 13, VOL. 64, No. 19, pp. 589-598 (*Bulletin of Hygiene*, Vol. 24, No. 11, November 1949, p. 838) .. 220

RELATION OF RELAPSES IN TYPHOID TO DURATION OF CHLORAMPHENICOL THERAPY. By J. E. Smadel et al. (*Journal of the American Medical Association*, Vol. 141, 10th September, 1949, p. 129) .. 220

TREATMENT OF HEPATIC AMOEBIASIS WITH CHLOROQUINE. By N. J. Conan (*American Journal of Medicine*, Vol. 6, March 1949, p. 309, as abstracted in the *Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 101) .. 221

AUREOMYCIN IN BRUCELLOSIS (*Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 106) .. 221

THIOARSENITES IN AMOEBIASIS. By H. H. Anderson et al. (*Journal of the American Medical Association*, Vol. 140, 20th August, 1949, p. 1251) .. 221

MYELOSCLEROSIS (*Lancet*, ii, 22nd October, 1949, p. 756) .. 222

POLIOMYELITIS AND TONSILLECTOMY (*Lancet*, ii, 3rd September, 1949, p. 424) .. 222

MYXŒDEMATOUS MADNESS. By R. Asher (*British Medical Journal*, ii, 10th September, 1949, p. 555) .. 222

(Continued on page 186)

CONTENTS—(Continued from page 185)

	Page		Page
STREPTOMYCIN TREATMENT OF INFANTILE DIARRHCEA AND VOMITING. By A. Holzel et al. (<i>British Medical Journal</i> , ii, 27th August, 1949, p. 454) ..	223	A TEXTBOOK OF PHYSIOLOGY. Originally by William H. Howell, M.D. Edited by John F. Fulton, M.D., Sterling Prof. of Physiology, Yale University Medical School. New Sixteenth Edition. 1949 ..	229
THEORIES OF THE ETIOLOGY OF CONGENITAL DEFORMITIES	223	THE CLINICAL EXAMINATION OF THE NERVOUS SYSTEM. By G. H. Monrad-Krohn, M.D., F.R.C.P. Ninth Edition. 1948	229
PROCAINE PENICILLIN WITH ALUMINUM MONOSTEARATE	224	AIDS TO FORENSIC MEDICINE AND TOXICOLOGY. By W. G. Aitchison Robertson, M.D., D.Sc., F.R.C.P.E. Edited by J. H. Ryffel, B.Ch., B.Sc., F.R.I.C. Twelfth Edition. 1949	229
CONTINUOUS INTRAVENOUS INJECTION OF TYPHOID VACCINE IN TREATMENT OF CERTAIN OPHTHALMIC DISEASES ..	224	BOOKS RECEIVED	229
FLOCCULATION TESTS IN THE DIAGNOSIS OF HEPATO-BILIARY DISEASE ..	224	ABSTRACTS FROM REPORTS ..	
CHOREA (SYDENHAM): A STUDY OF FIFTY-EIGHT ADDITIONAL PATIENTS ..	225	ANNUAL REPORT ON THE WORKING OF THE ASSAM MENTAL HOSPITAL, TEZPUR, FOR THE YEAR 1948. By Colonel A. N. Chopra, O.B.E., M.B., B.S. (Pb.), D.T.M. (Liv.), D.P.H. (Eng.), I.M.S. 1950	229
MUMPS MENINGOENCEPHALITIS WITH AND WITHOUT PAROTITIS	225	THE 83RD ANNUAL REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT, UNITED PROVINCES, AGRA, FOR THE YEAR ENDING 31ST DECEMBER, 1947	230
SCIENCE AND YOU. By Maurice Goldsmith (UNESCO Features, No. 17, 15th March, 1950, p. 10)	226	ADMINISTRATION REPORT FOR THE YEAR 1948-49. K. E. M. HOSPITAL AND G. S. M. COLLEGE	231
'POSITIVE CURE' CLAIMED FOR TUBERCULAR MENINGITIS (UNESCO Features, No. 17, 15th March, 1950, p. 9)	227	BRIEF REPORT ON HOSPITALS AND DISPENSARIES FOR THE YEARS 1941 TO 1945 TOGETHER WITH ANNUAL REPORT FOR THE YEAR ENDING 31ST DECEMBER, 1946. GOVERNMENT OF THE CENTRAL PROVINCES AND BERAR. GOVERNMENT PRINTING, C.P. AND BERAR, NAGPUR. 1949	232
REVIEWS		ANNUAL REPORT ON CIVIL HOSPITALS AND DISPENSARIES IN THE CENTRAL PROVINCES AND BERAR FOR THE YEAR ENDING 31ST DECEMBER, 1946	232
THE BRITISH PHARMACEUTICAL CODEX, 1949	227	CORRESPONDENCE	
PRACTICE OF ALLERGY. By Warren T. Vaughan, M.D. Revised by J. Harvey Black, M.D. Second Edition. 1948 ..	227	PENICILLIN AND SULPHADIAZINE IN LOBAR PNEUMONIA	233
PSYCHOSOMATIC MEDICINE: THE CLINICAL APPLICATION OF PSYCHOPATHOLOGY TO GENERAL MEDICAL PROBLEMS. By Edward Weiss, M.D., and O. S. English, M.D. Second Edition. 1949	228	HEPARIN IN YELLOW FEVER	233
MEDICAL ETYMOLOGY. By O. H. Perry Pepper, M.D. 1949	228	AN APPEAL	233
GENERAL CYTOLOGY. By E. D. P. De Robertis, M.D., W. W. Nowinski, Ph.D., and F. A. Saez, Ph.D. Translated by W. Andrew, Ph.D. 1948	228	I.M.G. PREVIOUS ISSUES	233
FEMALE SEX ENDOCRINOLOGY. By Charles H. Birnberg, M.D.	228	SERVICE NOTES	233
HYGIENE. By J. R. Currie, M.A. (Oxon.), M.D., LL.D. (Glas.), D.P.H. (Birm.), F.R.C.P. (Edin.), and A. G. Mearns, M.D., B.Sc. (Public Health), D.P.H. (Glas.), F.R.S. (Edin.). Third Edition. 1948	228		

Original Articles

GONOCOCCAL ARTHRITIS

By S. L. MALHOTRA, M.R.C.P. (Lond.), D.C.H. (Eng.)
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Railway

WITH the advent of penicillin and streptomycin, the treatment of gonococcal infections has undergone a further change in outlook. In the present paper the methods of treatment for gonococcal arthritis available at present are analysed.

Early and correct management of gonococcal arthritis is important for two reasons :—

1. That it is a destructive joint lesion and if not treated early it may lead to irreparable damage and disability.

2. That the common chemotherapeutic agents used for genito-urinary gonorrhoea are completely ineffective in its treatment.

Forty-six cases of gonococcal arthritis were studied for a period of one year on a follow-up and the results of treatment are reported.

Diagnosis

The diagnosis of the gonococcal nature of arthritis in this report is based on the repeated microscopic examinations of prostatic smears. This study is confined only to cases whose prostatic smears were positive. Attempts were also made to demonstrate gonococci from the joint effusions of the four cases who had such effusions with only one success.

During the bacteriological examinations of the prostatic secretions the frequent presence of secondary invaders mostly *B. coli* and streptococci was noted. In the writer's opinion this is a fact of great importance.

Methods of treatment used

Cases were divided into 4 groups in order to obtain a comparative analysis of the results :—

Group A.—Treated with combined chemotherapy with sulphathiazole and penicillin but without pyretotherapy.

Group B.—Treated with sulphathiazole and hyperpyrexia.

Group C.—Treated with penicillin and hyperpyrexia.

Group D.—Treated with streptomycin followed by penicillin.

Results

Group A.—Group A had 26 cases who received a combined course of penicillin and sulphathiazole on the following dosage schedule : Penicillin, 40,000 units by three-hourly intramuscular injections for five days, combined with

sulphathiazole 6 gm. daily by mouth in 4 divided doses for six days.

It was noticed that only 6 cases were relieved (3 cured and 3 improved) under this treatment. The other 20 cases in which the treatment proved a failure were divided into two groups of 10 each, one of these groups was included in group B and the other in group C. The failure of penicillin and sulphathiazole as a therapy in this series is noteworthy.

Group B.—This includes 10 new cases and the 10 failures of group A. They were treated with pyretotherapy and sulphathiazole. Pyretotherapy was induced by intravenous T.A.B., producing three febrile bouts of a temperature range between 103° and 105°F. This was continued with three more febrile bouts produced by Bircher-Challenger model short-wave diathermy unit, producing a temperature range from 104° to 105°F. for a period of 5 hours each. There were no remote ill-effects of the hyperpyrexia but a few of the cases tended to become boisterous at a temperature between 101° and 102°F. A few others complained of an uncomfortable feeling of heat and burning on the back close to the cable. Ten cases were completely cured and four improved. Six cases did not respond, out of which two had advanced joint change in which improvement could not be expected.

Group C.—Includes 10 new cases and 10 failures of group A. This group was treated with hyperpyrexia as in group B, plus penicillin : a total of 400,000 units spread over 3 days. The results are tabulated : 11 cases were completely cured and 4 were improved.

Group D.—This includes the 4 failures of group B and 1 of group C and 4 new cases whose prostatic secretions also showed evidence of secondary organisms. They were treated with a three-day course of streptomycin followed by penicillin as in group C. Dosage used being 0.5 gm. of streptomycin by six-hourly parenteral route. There were no failures in this group. It is noted that hyperpyrexia was not used in this group. With this short course of streptomycin although a slight improvement was evident in nearly all the cases of the group, complete subsidence of the joint condition was brought about by penicillin.

Comments

1. The failure of chemotherapy and penicillin in the treatment of gonococcal arthritis without adjuvant hyperpyrexia is noteworthy.

2. Equally noteworthy is the presence of secondary organisms mostly *B. coli* and streptococci in the prostatic secretions. These stand out conspicuously even in the ordinary stained smears distinct from gonococci in morphology. Identity was confirmed by culture.

3. Cases in group D strongly suggest that secondary invaders may protect the gonococci

		Number of cases treated	Number of cases showing evidence of secondary infection	Number of cases cured	Number of cases improved	Number of failures	Number of cases in which improvement could not be expected due to advanced joint destruction
Group A	..	26	8	3	3	20	Nil
Group B	..	10 + 10 (failures of group A).	10	10	4	4	2
Group C	..	10 + 10 (failures of group A).	4	11	4	5	Nil
Group D	..	7	5	7	Nil

from the action of penicillin and sulphathiazole and that once they are eradicated with streptomycin the gonococci are quickly eliminated by these drugs from the prostatic smears. The importance of secondary organisms is well known especially in amœbiasis and it is now an accepted procedure in the treatment of amœbiasis to eliminate the secondary infection before giving anti-amœbic treatment. However, it is also probable that streptomycin may be exerting its own gonococcocidal action in addition to its rôle of eradicating secondary invaders.*

4. Hyperpyrexia seems to be a necessary adjuvant in the treatment of gonococcal arthritis as can be seen from the statistical analysis. But the possibility that an initial course of streptomycin may ultimately dispense with hyperpyrexia is apparent from the observation in group D. It will, however, be necessary to have a larger number of cases treated on this plan before a final pronouncement can be given.

Conclusions

1. Treatment of 46 smear-positive cases of gonococcal arthritis is given.

2. The importance of secondary infection with *B. coli* and streptococci in prostatic secretions with its repercussions on treatment is discussed.

3. It is suggested that a preliminary course of streptomycin to eliminate the secondary organisms may completely dispense with pyretotherapy as an essential part of treatment, thus simplifying the treatment of gonococcal arthritis.

I am grateful to Dr. S. B. Sen Gupta, M.B., D.T.M., for help in the laboratory work, and to my chief Dr. S. N. Lahiri for permission to send this communication.

*The writer has similarly noticed a less dramatic response with penicillin in genito-urinary gonorrhœa than reported in the literature. Pus discharge from prostatic smears had similarly shown the presence of secondary organisms in some of the cases. A 5-day course of streptomycin failed to produce cure in the 3 cases in which it was tried but when followed with penicillin the response was quick. The writer believes that secondary infection is nearly always present although it may not always be possible to demonstrate it. The importance of eradicating this is emphasized before instituting specific medications.

DISSEMINATED LUPUS ERYTHEMATOSUS

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LUPUS ERYTHEMATOSUS was first described by Beitt (1828) as 'Erythema centrifuge'. Hebra in 1845 described the disease and it was then considered as a specific dermatological affection. Kaposi (1872) and Osler (1895) were the earliest to recognize that the skin changes in this disease had their counterpart in the internal organs. As Kaposi states 'Lupus erythematosus may also appear as a disseminated or generalized acute or subacute febrile eruption and in such circumstances intense local and constitutional symptoms may affect the organism and may even endanger or destroy the life of the patient'. While he noted that the primary cutaneous manifestation was identical in the chronic and acute types, he believed that there was a fundamental difference in the morbid process as it affected the organism in the two types. The existence of this acute form of lupus was not generally recognized by dermatologists until when in 1904 Jadassohn (1904) summarizing contemporary dermatological experience recognized acute lupus erythematosus as a constitutional disease and noted joint symptoms, glandular swellings and particularly renal involvement. More recently the systemic manifestations of acute lupus erythematosus have received more consideration than the dermatological aspects.

The pathological changes in the disease have been exhaustively reviewed by Klemperer *et al.* (1941). The ætiology of the disease is not definitely known. It seems it has some relation to tuberculous or some septic focus in the body, usually due to *Streptococcus hæmolyticus*. The disease has on rare occasions been precipitated by injections of therapeutic sera (Fox, 1943). Hypersensitivity to Rh and other red cell antigens has occasionally been noted. External irritations like sunlight or cold wind may

worsen skin manifestations. The favoured view is that it is an allergic manifestation to tubercle bacillus, hæmolytic streptococcus or to some unknown agent.

The essential pathological change is fibrinoid degeneration of collagen fibres, lesions being found not only in vessel wall and skin but in many other sites like heart, kidneys, lungs, retina and serous surfaces like pleura, peritoneum and pericardium.

The disease is almost always confined to the female sex during the child-bearing age.

The initial manifestations of the disease are of interest. Tumulty and Harvey (1949) note that in only a little over one-third of the cases, the characteristic skin changes are present at the onset. Typically these consist of a macular erythematous rash with sharp margins. They are characteristically distributed over the nose and prominences of the cheek, producing butterfly or bat's wing appearance. The rash is present also in other areas of the body like scalp, forearms, hands, chest, back and lower extremities. Sometimes bullæ may appear and hæmorrhage may occur in the rash. Atypical cases may show purpura, cutaneous pigmentation or urticaria. The oral mucous membrane may show ulcerations. The rash may precede, accompany or succeed the visceral and constitutional manifestations and in some cases may even be absent altogether.

Equally common is an initial complaint of pain in joints of rheumatoid character. Less often patients may have unexplained fever and weakness, loss of weight, gastro-intestinal disturbances and hæmorrhagic phenomena as presenting features.

The clinical features of the disease are varied and complex, depending on the involvement of different organs. Fever is constantly present in the acute stage and may be accompanied by chills.

The joint pains are often migratory in character and occur in episodes separated by free intervals of months or years. The affected joints may show inflammatory signs and deformities. Sometimes ankylosis, contracture and neighbouring muscle atrophy may be present. The appearances may be indistinguishable from rheumatoid arthritis. Sometimes in spite of marked arthralgia no changes may be found in the joints.

Much attention has been paid to cardiac affection in this condition. Osler described one case complicated by acute endocarditis and referred to other instances in the literature. Libman and Sacks (1924) described four cases under the title 'A hitherto undescribed form of valvular and mural endocarditis', two with and two without skin manifestations but all had a form of endocarditis designated as atypical verrucous endocarditis. The finding is usually a post-mortem one and is unlikely to

lead to heart failure. A soft apical systolic bruit has been noted by various writers. Secondary bacterial endocarditis superimposed on a valve previously damaged has been reported by Tumulty and Harvey (1949). Myocardial scarring secondary to arteritis and ischæmic necrosis of the myocardium are other pathological findings of interest.

The frequency of gastro-intestinal manifestations was stressed by Osler (1895, 1900, 1903). Subsequent writers do not appear to have paid much attention to them. Tumulty and Harvey (1949), however, support Osler's observation and have noted diarrhoea frequently with blood in the stool and abdominal cramps. The case reported by us had, during observation, an episode of unexplained nausea, vomiting and upper abdominal pain.

Enlargement of the liver has been frequently noted both clinically and at post-mortem examinations. In most instances this is due to deposition of large amount of fat and only occasionally hepatic necrosis is found. Hepatic functions have been studied by a few writers and abnormal results have been found in all instances. Our case showed slight enlargement of the liver and the liver function tests showed evidence of impaired function. Pathological changes characteristic of disseminated lupus erythematosus have never been demonstrated in the liver.

Enlargement of the spleen has been noted in less than half the cases. In Indian subjects much stress cannot be laid on splenic enlargement owing to the diverse causes of splenomegaly.

Osler (1895, 1900, 1903) noted the association of lupus erythematosus with thrombocytopenic purpura and similar cases have been subsequently reported (Lyon, 1933; Keil, 1937). Thrombocytopenia is regarded by some as a characteristic feature of the disease. Leucopenia has also been frequently encountered. These together with anaemia which is often associated give the impression of a general depression of the whole hæmopoietic system. Pancytopenia was noted as a feature in our case. Generalized lymphadenopathy or adenopathy limited to cervical and axillary glands has been described by some.

Autopsy examinations have revealed the frequency of the specific changes of lupus erythematosus in the kidney even when no clinical abnormality is detected. An abnormal urinary finding with or without evidence of impairment of renal function, and sometimes a significant degree of azotæmia may be found.

Pulmonary manifestations during the course of lupus erythematosus have been emphasized. In Tumulty and Harvey's (1949) series pneumonia was the commonest finding, often a terminal event. Empyema and lung abscess were seen, while pulmonary tuberculosis was present in only two out of thirty-two cases. In

one instance only, x-ray revealed a non-tuberculous type of infiltration throughout both lung fields, which at autopsy was found to be produced by small scattered areas of lung containing the typical lesions of lupus erythematosus. In our case the skiagram of chest showed diffuse minute mottlings over both lungs.

Involvement of serous membranes producing pericarditis and pleurisy with or without effusion is said to occur commonly. Mild perisplenitis and perihepatitis have also been noted at autopsy. Ascites is rare except in association with general anasarca.

Neurological manifestations attributable to lesions of lupus erythematosus in the central nervous system are not infrequent. Transient periods of coma, generalized convulsions, hemiplegia, and toxic psychosis have been described. In some instances, delirium, coma or convulsive episodes may be due to uræmia.

Maumenee (1940) described retinal lesions in four cases of acute lupus erythematosus. He noted small fluffy white spots located in the posterior part of the disc, very similar to the exudates in hypertensive retinopathy. Histologically they are shown to be areas of cytooid bodies. He also noticed small hæmorrhages which were not related to the white patches or to large retinal vessels and those were seen microscopically to lie in the nerve fibre layer of the retina. These ophthalmoscopic appearances are not specific, but in absence of hypertension, they provide a valuable clue specially when visceral manifestations are present without skin changes.

Biochemical studies in this disease have attracted some attention. Coburn and Moore (1943) have noted that hyperglobulinæmia is a constant characteristic of the lupus state. Electrophoretic analysis reveals that the globulin increase is chiefly due to the gamma globulin fraction. There seems to be a tendency for serum globulin to be highest in those patients showing the most marked arthritic manifestations. In our patient there was hyperglobulinæmia.

It is relatively easy to make the diagnosis of disseminated lupus erythematosus when the patient shows all the characteristic manifestations including fever, arthritis, cutaneous lesions, sterile effusion in serous cavities and the picture of chronic nephritis. Course of the disease is characterized by fluctuations in the degree of activity. In about 50 per cent of cases the course is acute with high fever and toxæmia. The mortality rate is very high in them. In the rest of the cases recovery may take place, though the course may be prolonged for several months or years with occasional bouts of irregular fever, joint pains and rash. Different features may appear in successive attacks. In this way the full picture of the disease may only unfold in the course of years. Once the diagnosis is clear

the tendency is to attribute any and every symptom to the disease. Every symptom must be viewed with an open mind and assessed at its proper perspective.

The disease is rare enough to make this case worth publishing.

The case

Mrs. P. B., Hindu female, aged 35 years, was admitted in the Campbell Hospital under one of us (N. R. K.) on 15th September, 1949, with a history of pain in joints and irregular fever for 4 years and pink rash over face, arms forearms, back and chest for 9 months. The present illness started 4 years ago when the patient had pain on the left side of the neck. The pain later spread to the outer side of left arm and forearm and lasted for 4 months. It was dull aching in character and increased on movements. She was free from pain for about 2 months. The left knee joint then became painful and the right one was subsequently affected. She used to get low irregular fever along with the pain in the joints. There was no chill or rigor. Parenteral penicillin controlled the fever and the pain in the joints became less.

The rash first appeared over the upper lip as raised pink spots. Further rash appeared over the face, eye-lids, inner surface of the pinna, scalp, lower part of neck, chest, back, arms and forearms. The spots never appeared on the abdominal wall or on the lower limbs. They were reddish in colour, raised above the surface, roughly 0.25 to 1 cm. in diameter. They were covered with rather firmly adherent scales, which when scrapped off did not leave punctate hæmorrhagic spots. There was no pain, tenderness or irritation in them. While in hospital, a few went to pustule formation, apparently due to secondary infection and they responded to penicillin. There was no bulbous formation nor any hæmorrhage in the rashes. On subsidence of the acuteness of the disease the rash became darker in colour and depressed below the level of the skin leaving blackish pitted areas. The spots were most profuse over the nose and prominence of the cheek bones producing typical bat's wing or butterfly appearance (figure 1, plate XXXI). On admission, in addition to low irregular fever, joint pain and rash over the body, she complained of palpitation, dry cough, pain over the right side of the chest and slight dyspnoea.

Family history.—History of pulmonary tuberculosis in mother-in-law.

Past history.—Small-pox in childhood and occasional attacks of malaria.

Personal history.—She has been married for 18 years. No issue.

On examination.—The patient was moderately built. There was no jaundice, cedema or glandular enlargement. Anæmia was moderate. Tongue was slightly coated and moist. Teeth and gums looked healthy. Tonsils and fauces

were congested. No abnormality was detected in heart and lungs. Temperature was 100°F . Pulse was 110 and respiration was 24 per minute. Blood pressure: systolic 98, diastolic 68 mm. of Hg. Liver was just palpable. It was soft in consistency. No tenderness was present. Spleen was palpable three fingers breadth below costal arch. It was hard in consistency and was not tender. The character of the rash has already been described. The patient complained of pain in both knee joints which increased on movement and weight bearing. There was some tenderness over them. No other abnormality was detected. Other joints were healthy.

Laboratory investigations.—Blood: Hb. 54 per cent (7.89 gm. per 100 ml. of blood); R.B.C. 2,180,000 per c.mm.; W.B.C. 3,200 per c.mm.; polymorphonuclear cells 66 per cent, lymphocytes 22 per cent; monocytes 10 per cent; eosinophils 2 per cent; platelets 111,180 per c.mm. Protein content of blood: albumen 3.2 gm. per 100 ml., globulin 3.6 gm. per 100 ml., total 6.8 gm. per 100 ml. E.S.R. 61 mm. per hour (Westergren). Blood W.R.: doubtful. Complement fixation test for kala-azar: negative. Aldehyde test: negative. Stool: no abnormality. Urine: small amount of albumen without any casts or red cells. Sputum: acid-fast bacilli not found. *Streptococcus hemolyticus* was grown from throat swab.

Mantoux test: strongly positive in 1 in 1,000 dilution. Liver function tests: intravenous hippuric acid synthesis test. (Quick): 0.629 gm. hippuric acid excretion (normal mean = 1.01 gm.). Cephalin cholesterol flocculation test: ++ (normal 0 to +). Blood urea: 36.5 mg. per 100 ml.

N.P.N: 36.0 mg. per 100 ml. Biopsy of a spot on forearm. Thickening of epidermis, follicular plugging, dilated blood vessels and œdema of dermis. Lymphocytic infiltration is not much evident in this picture (figure 2, plate XXXI).

X-ray knee joint: normal appearance. Chest: diffuse minute mottling over both lungs (figure 3, plate XXXI).

Heart: normal. E.C.G.: P.R. interval, 12 second P3 T3 inverted with bizarre type of Q.R.S. Conclusion: no abnormality detected in

heart on radiological or electrocardiographic examination.

Clinical course.—The patient was admitted on 15th September, 1949, with a temperature of 100°F . and pain in both knee joints. The temperature was irregular and varied between 98.4°F . and 100.5°F . (figure 4). She was put on intramuscular injections of penicillin, 50,000 units, 6-hourly on 21st September, 1949. The temperature came down to normal on 28th September 1949, and the penicillin was omitted on 1st October, 1949. The temperature rose to 100°F . on the next day and varied between 98.4°F . and 102°F . She was again put on penicillin on 3rd October, 1949, on similar doses as on previous occasion. The temperature came down and has remained at normal level since 7th October, 1949. The penicillin was continued till 14th October, 1949; total amount given in 21 days being 4,100,000 units. During the bout of fever between 2nd October, 1949, and 6th October, 1949, she vomited several times and complained of pain in epigastrium. Since her admission in the hospital no fresh crop of rash has appeared and she feels better after the course of penicillin. The rash has become darker in colour and depressed below the surface of the skin. Some pitting could be seen specially over the nose. She had an attack of diarrhoea on 17th October, 1949, which responded to sulphaguanidine and restricted diet. She was put on quinine sulphate gr. 7, thrice daily, which was later reduced to twice daily, as the patient complained of tinnitus, nausea and vomiting. It did not produce any effect on the disease. Later she has again been complaining of pain in both knee joints. There is some tenderness in them and the pain increases on movement and weight bearing. No fluid could be detected in the joints. She states that it has been her experience for the last 4 years to notice improvement in rash, fever and pain in joints with penicillin, but there has always been relapses after intervals varying from weeks to months. Later she has been put on injections of bismuth, with no effect on the clinical course of the disease. Full effect of gold on this case could not be tried, as one intramuscular injection of it produced urticarial rash all over the body.

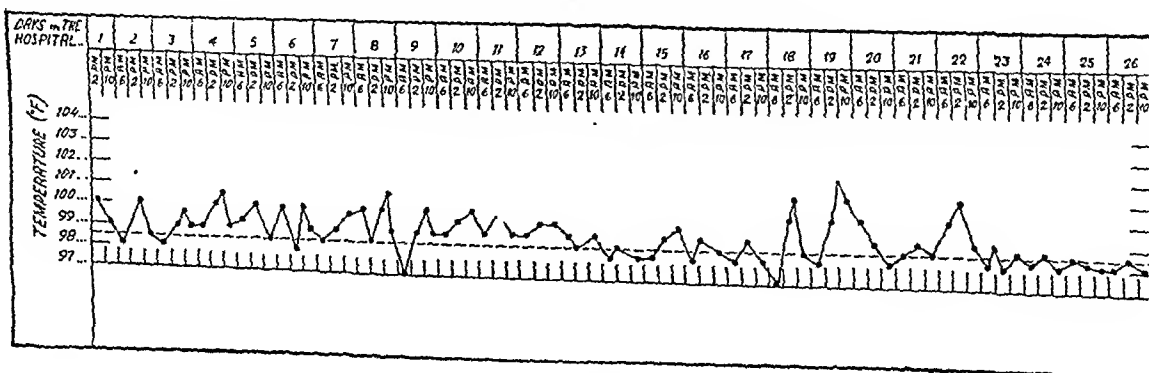


Fig. 4.

Discussion

The most distressing symptom in this case was repeated attacks of pain in both knee joints, but the conspicuous feature was rash over the face. The patient had bouts of irregular fever along with pain in the joints. No definite abnormality was detected in the joints on clinical or radiological examinations. Fever and pain in joints always responded to penicillin, but drugs like salicylates, aspirin, bromides, quinine and bismuth had no effect on them. The spleen was enlarged which could be explained by previous attacks of malaria. There were anaemia, leucopænia and thrombocytopænia. Globulin content of blood was raised and erythrocyte sedimentation rate was high. Mantoux test was strongly positive to 1 in 1,000. Throat swab showed *Streptococcus hemolyticus*. Skiagram of chest showed diffuse mottling. Hippuric acid synthesis and cephalin cholesterol flocculation test showed defective hepatic function. No abnormality was detected in heart and retina.

In psoriasis arthropathica typical changes of rheumatoid arthritis are usually found in the joints. Moreover the rash had neither the character nor the distribution of psoriasis. To determine if the clinical condition could be due to some toxic effect of drugs, she was put on salicylates, aspirin, bromides and sulphonamide group of drugs. They had no effect on the clinical course of the disease.

Summary

A case of disseminated lupus erythematosus has been described.

The literature on the subject has been reviewed.

Penicillin produced clinical improvement in fever and joint pain but did not prevent relapses.

Salicylates, aspirin, bromides, bismuth, quinine and sulphonamide group of drugs had no effect on the disease.

Our thanks are due to Dr. A. K. Dutta Gupta, Superintendent, Campbell Medical School and Hospitals for the permission to report this case, Major A. Chakrabarty, Visiting Physician-in-charge of the Skin Department, Medical College Hospitals for the help in the diagnosis of the case, Dr. J. B. Chatterjee for hæmatological reports, Dr. H. Chakravorty for estimation of plasma protein and Major H. Sinha for the report on the culture of throat swab.

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POST-NECROTIC SCARRING OF THE LIVER IN A CHILD AND ITS POSSIBLE RELATIONSHIP TO Rh FACTOR

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POST-NECROTIC scarring is a condition in which the liver shows subacute necrotic changes, gross deformation and produces large irregular nodules circumscribed by broad bands of connective tissue. The distinctive feature of this type of cirrhosis was first described by Mallory (1911) who named it 'toxic cirrhosis'. The name 'multiple nodular hyperplasia' has been given to a similar condition resulting from subacute yellow atrophy. The multilobular appearance is considered by Himsworth (1947) to be a distinctive feature of post-necrotic scarring. It is a sequel of subacute massive hepatitis whether it arises in acute process or insidiously. Glynn and Himsworth (1944) and Glynn, Himsworth and Neuberger (1945) have demonstrated in experimental rats that the dietetic deficiency of sulphur containing amino-acid cystin resulted in an acute massive hepatic necrosis after a latent period and the survivors of which developed post-necrotic scarring and nodular hyperplasia. In human beings it most commonly arises spontaneously or in association with pregnancy toxæmia but may also arise during the therapeutic administration of certain organic chemical substance, e.g. cinchophen, or may follow poisoning by certain industrial chemicals, e.g. trinitrotoluene. So naturally the cause may be due to two factors, trophopathic and toxipathic. Karsner (quoted by Lichtman, 1949) observed that post-necrotic scarring affects females more than males and although it may occur at any time of life, it is likely to affect younger age groups more than other forms of cirrhosis.

✓ Recently we have observed in the autopsy on a child hepatic lesions which are typical or simulates post-necrotic scarring of the liver, in which Rh isoimmunization of mother has also been observed. So the question of possible relationship between the two conditions is

thought of and the case is being reported in detail.

Case report

D. B., a Hindu male, Brahmin by caste, aged 4½ years, was admitted into the Medical College Hospital on 20th April, 1949, for low irregular fever, loss of appetite, gradual weakness and loss of weight—3 months, gradually deepening yellowish coloration of conjunctiva and skin—1½ months.

The patient was the fourth child in a family of six children born at term, and fed on the breast up to 5 months and then given artificial feed and brought up on mixed diet. Parents are healthy. Mother had never any blood transfusion in her life.

First child—a boy, died at the age of 5 years, the course of the disease was of 3 months' duration with symptoms of gradual weakness, low fever, in ascites and œdema legs, the death caused by severe hæmorrhage per rectum.

Second child—a girl, died at the age of 4 years, the course of the disease was 2 months with symptoms like the first child and death caused by severe terminal hæmatemesis.

count 11,100/c.mm. Neutrophils 82 per cent. Lymphocytes 17 per cent. Monocytes 1 per cent. Eosinophils nil. M.P. nil. Aldehyde and Chopra tests negative. Urine showed a trace of albumin, bile salts and pigments, and a few pus cells on microscopic examination. Stool was yellowish, semi-solid, but no abnormality was found. Van den Bergh reaction immediate direct positive. Icterus index 200. Bilirubin content 18 units. Fasting blood sugar 70 mg./100 cc.; glucose tolerance test within normal limits. Red cell fragility started at 46 per cent and completed at 38 per cent of sodium chloride solution. Protein content of ascitic fluid was 18 per cent. W.R. of the patient as well of the parents was found to be negative. The exclusion of lentic infection suggested an unknown toxin acting slowly from the very inception of life in every child of the mother leading to the typical cirrhotic condition. Hence an Rh determination of blood was undertaken. The father was found to be Rh₀ positive, mother Rh₀ negative. The patient was found to be Rh₀ positive.

Subsequent to the death of the child an Rh-Hr typing and blood grouping of the family were done and results were as follows :

Name	Age in years	Group	REACTIONS WITH ANTISERA						GENOTYPE	
			Rh' C	Rh ₀ D	Rh'' E	HR' c	HR ₀ d	HR'' e	Weiner's nomenclature	Fisher's nomenclature
Father	36	O	+	+	—	+	R ₀ r	CDe
Mother	30	A	+	—	—	+	R'r	cde
Daughter (5th child) ..	2½	A	+	+	—	+	R ₀ r	CDe
Son (6th child) ..	11 months	A	+	+	—	+	Do.	cde
										Do.

Third child—a boy, died at the age of 5 years, the course of the disease was of 3 months with similar symptoms as the first and second child with terminal melæna.

Fifth child—a girl, aged 2½ years, living, healthy and well nourished.

Sixth child—a boy, aged 11 months, living, healthy.

Examination.—The child was fairly well nourished with moderate jaundice of all visible mucous membranes and skin. The abdomen was moderately distended. Veins around umbilicus were slightly prominent. Liver was felt 3.5 cm. below costal margin, firm to feel but not tender. Spleen was just palpable. Free fluid was present in the abdomen. Rectal examination showed no abnormality. In the heart soft systolic murmur over mitral and pulmonary area was elicited. Lungs were normal.

Laboratory findings.—Hæmoglobin was 32 per cent. R.B.C. 1.8 million/c.mm., white cell

Progress of the case.—On 26th April, 1949, the abdominal distension increased causing distress to the patient. 44 oz. of bile strained fluid were removed by paracentesis. Again 50 oz. of fluid were removed on 30th April, 1949. Patient developed extreme anorexia. On 3rd May, 1949, he had hæmorrhagic stools, complained of pain in the right hypochondrium, became gradually drowsy and died on 6th May, 1949, from a terminal severe hæmatemesis.

During the stay in hospital the patient had an irregular temperature varying between 98°F. and 103°F., remittent and at times intermittent.

Autopsy findings.—Post-mortem examination was held 23 hours after death, the body being preserved in the cold chamber. The body was fairly well developed and nourished with skin and mucosa very pale and moderately bile coloured. Prominent tortuous veins were visible beneath the skin of the abdominal wall.

On opening the abdomen peritoneal cavity was found to contain 4 oz. of hæmorrhagic fluid. Liver was 420 gm. in weight, yellowish brown in colour, 15 cm. \times 11 cm. \times 6 cm. The whole organ was irregularly nodular on the surface (figure 1, plate XXXII). Consistency was firm and the texture resistant to cutting. The cut surface showed yellowish areas separated by greyish white connective tissue. The gall-bladder was normal in size and healthy. All ducts were patent. Spleen was 70 gm. in weight, normal. Lower end of œsophagus contained several dilated tortuous vessels. The site of rupture of the varicose vessel which resulted in final hæmorrhage could not be traced. Pancreas was moderately firm to the feel and its surface normal. Cut surface showed round yellowish areas surrounded by greyish tissue. Kidneys were normal. Lungs: left lung was normal; right lung showed minute hæmorrhages in the margin of the lower lobe under the visceral pleura. Heart was normal. Brain showed no evidence of bile staining. Bone marrow of femur was red and appeared normal. Histologically the liver showed extensive necrotic changes in hepatic cells, fibrous tissue multilobular in its distribution (figure 2, plate XXXII) and proliferation of the biliary capillaries (figure 3, plate XXXII). No other organ showed any significant change excepting the pancreas which showed fibrosis.

Discussion

It is generally known that erythroblastosis fœtalis may be associated with slight or moderate hepatomegaly and splenomegaly due to excessive blood destruction which disappears as the child grows up. The question arose whether Rh isoimmunization of the mother had any rôle in the causation of parenchymatous damage of liver and spleen in children.

Search of literature shows observations by workers on Rh on this aspect of the factor. Henderson (1942) reported an increase of fine intralobular connective tissue in the livers of still-births, who died of hæmolytic disease. Drummond and Watkins (1946) reported hepatomegaly and splenomegaly in three out of five siblings of a family where Rh isoimmunization of mother's blood has been proved. Before the discovery of Rh, Braid and Ebbs (1937) found atrophic cirrhosis in a child, who died at the age of 3½ years following icterus gravis neonatorum.

The parents in this family never noticed any jaundice in their children at birth or soon after. This is in conformity with the findings in the cases of Nussey (1949) and Drummond and Watkins (1946).

Two points must be considered: (1) Can Rh incompatibility cause symptoms of parenchymatous damage of liver without any evidence of hæmolysis in the blood of infants, e.g. hydrops fœtalis and icterus gravis neonatorum? (2) If so, how is the parenchymatous damage caused?

Investigations by Vaughan (1946) have shown that kernicterus is not found in cases of intense jaundice associated with diseases other than erythroblastosis fœtalis. In this disease, the basal ganglia, composed of highly specialized nerve tissue, are affected. The nerve cells of the basal ganglia undergo degeneration and atrophy manifested clinically by mental impairment and spastic paresis as the child grows up.

Symptoms of kernicterus may occur in children who had no jaundice. There is no relation between kernicterus and degree of blood destruction. Probably kernicterus is the result of a cell-destructive process similar to that by which the red blood cells are destroyed, in other words, an antigen antibody reaction in the tissue. Boorman and Dodd (1943) have shown evidence of presence of Rh group specific substance in liver, spleen, kidney, etc. It seems plausible that liver tissue, where Rh specificity is a protoplasmic characteristic, should be held susceptible to injury by Rh antibody like the nerve cells.

The second point of interest in the case reported above is the familial trait of the disease. Cirrhosis of the liver in children with hereditary tendency where several children of a mother suffer from the malady as each reaches the critical age has been thought to be common in India. Familial hepatic cirrhosis in children has also been reported by European and American writers. Weber (1903), Debré (1939), Weber (1936), Langmead (1934), Bridgeman and Robertson (1932) and Sutton (1930) reported cases of atrophic cirrhosis in children with hereditary tendency. The pathogenesis of familial hepatic cirrhosis in children of healthy parents may be due to a toxic action on liver cells, but the real toxin could not be discovered. At least in some of the cases the answer might well come from Rh specific substances combining with antibody, causing necrosis of parenchymal cells of liver and the evolution of cirrhosis.

Rao (1935) studied the morbid condition of the liver in the disease commonly described as biliary cirrhosis in Indian children and labelled them as 'subacute toxic cirrhosis' manifesting biliary inflammation in rare cases. In the case reported above besides the necrosis and multilobular fibrosis there was marked proliferation of the biliary capillaries. This biliary proliferation has been noted by Glynn and Himsforth (1944) in post-necrotic scarring in experimental rats.

Structurally the histopathology of the so-called infantile biliary cirrhosis shows pericellular and interlobular fibrosis and the liver cell shows necrosis (a sort of subacute hepatic necrosis). The case of post-necrotic scarring being reported by us is structurally multilobular and the liver cells showed necrosis. A similar toxic ætiological factor might well be suggested and an Rh investigation may be undertaken in all cases of infantile cirrhosis.

Summary and conclusion

A family is reported in which the first four children have died of cirrhosis of the liver as could be gathered from the history, more or less at the same age period, suffering practically from the same type of illness, and all terminating in hæmorrhage from the gastro-intestinal tract.

Autopsy on the fourth child, in whom Rh isoimmunization of the mother was present, revealed primary hepatic cirrhosis (post-necrotic scarring). The association of Rh incompatibility in post-necrotic scarring in children has been stressed.

The post-mortem examination was allowed and this was only made possible by the interest taken by Dr. K. C. Chowdhury, the Chief Physician of the Children Hospital, Medical College, to whom our thanks are due. Our thanks are also due to Dr. A. Sen, Blood Transfusion Officer, West Bengal, for the blood groupings and Rh investigations done in the case, and to the Superintendent, Medical College Hospitals, for the records.

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CONGENITAL ATONIC DIPLEGIA

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HYPOTONIA in cerebral diplegia is relatively rare and when present is often associated with

choreo-athetotic movements and is present in the peripheral segments in between tonic spasms.

Cases with marked inco-ordination and hypotonia are due to a cerebellar component. Wilson (1940) divides such cases into three types:

(1) Diplegia with cerebellar symptoms: cerebro-cerebellar diplegia.

(2) Atonic diplegia (atonic-astasia type of Foerester).

(3) Cerebellar diplegia (congenital cerebellar ataxia of Batten).

He includes all these under the heading of cerebellar diplegia. But, to quote the same author, Wilson (1940): 'The asynergy is doubtless cerebellar, but whether abnormal limb excursions and joint extensibility, as well as loss of tone, are more than an extreme degree of what can be found in distal parts of infantile (cerebral) hemiplegia or diplegia limbs is not altogether clear'.

Brain (1947) does not mention atonic diplegia but probably includes it in his cases of cerebellar diplegia covering those which show hypotonia and ataxia.

Ford (1945), on the other hand, while describing in detail congenital atonic diplegia and quoting cases of others as well as his own, distinguishes it from cases of congenital cerebellar ataxia because of greater loss of muscle tone, less evident inco-ordination and the greater defect of mentality in the former, though he admits the difficulty in differential diagnosis between the two.

A case of congenital atonic diplegia is being reported in detail. Along with this, there were microcephaly, plagiocephaly and a gross mental defect.

Case report

R., 9 years old male child, was admitted on 11th October, 1949, into the Medical College Hospital with the complaints of inability to walk and talk. He was the first child of young parents and was one of the twins, the other, also male, having died on the 8th day due to imperforate anus. The child had been weak from birth. Labour was full-term and unaided. No history of injury. He used to lie very quiet and still for the first two months of life. After that, he started putting his limbs across each other with constant movements which are said to have stopped with massage. Birth weight not known. He had one sister whose development was normal.

Physical examination revealed thin, lean, poorly developed child. Height 42 inches and weight 29 lb. 4 oz. on admission. Looked like an idiot (figures 1 and 2, plate XXXIII). Could not talk but made unintelligible noises when excited, emotional display exaggerated. Some dribbling of saliva. Skull circumference eighteen and a half inches and showed flattening at the back and on left side (figure 3, plate XXXIII). All the muscles were weak and poorly developed. There was gross hypotonia in the

muscles of the neck, trunk and the upper limbs (figure 4, plate XXXIII). In the lower limbs there was some increase of tone in the adductors of the thigh and to some extent in the calf muscles best shown on holding the child from the axillae and suspending (suspension test—Ford, 1945; figure 5, plate XXXIV) when there was extension of the knees, plantar flexion of the feet and tendency towards crossing of the limbs. But, when the child was put on the floor, he was unable to maintain his weight and collapsed. On attempting to make him sit up, the head fell backwards, the trunk stooped forward and the child was unable to sit unsupported. Co-ordination was poor. The child made swaying movements of the hand when trying to reach an object and the movement spread all over the body. During these attempts the hand was often flexed at the wrist and hyperextended at the metacarpophalangeal joints, very much like the outstretched hands in a case of chorea. There were also choreiform movements in the hands and feet, more marked when excited or being watched and disappearing when asleep.

Intelligence poor. Hearing good. Could understand simple questions but could not speak. Emotional lability and expression increased. Cranial nerves: nothing abnormal. Fundus: nothing abnormal. Sensations: normal.

Superficial reflexes: corneal and pupillary, present; abdominals, brisk; plantars, flexor. Tendon jerks: all present, not increased. Autonomic reflexes: Got choking sometimes while swallowing. Had no control over micturition and defaecation.

No other abnormality in any other system.

Clinical impression: Congenital atonic diplegia; congenital cerebellar ataxia?; amyotonia congenita?; Arnold-Chiari syndrome and platybasia?

Consolidated investigation report:—

Skiagram skull—left lateral (figure 6, plate XXXIV)—shows flattening of the skull at the back. A line drawn from the posterior border of the foramen magnum runs about half an inch above the apex of the odontoid process. No signs of increased intracranial pressure.

Air-encephalogram (after injection of 50 cc. of air into the cisterna magna through subarachnoid puncture) (figure 7, plate XXXIV). Report by the radiologist, Dr. T. C. Wasson:

'The following subarachnoid spaces are outlined. 1. Frontal, 2. Temporal and 3. Occipital.

Frontal: Three gyri can be visualized (figure 8, plate XXXIV). Superior, middle and inferior.

Occipital and temporal show no gyri.

Frontal gyri can be seen in a good number of pneumo-encephalograms normally. The occipital subarachnoid space is generally visualized in cases of hypoplasia of cerebellum'.

W.R. (blood): negative.

Lumbar puncture showed clear watery C.S. fluid, not under tension, containing: total proteins 8 mg./100 cc. chlorides, 700 mg./100 cc. W.R. negative.

Urine did not contain any phenyl pyruvic acid.

Muscles showed normal electrical reactions. Muscle biopsy from the leg muscles showed normal striped muscle tissue. The report of the pathologist (Dr. G. L. Sharma) was:

'There are no abnormal alterations affecting the muscle fibres except their separation by oedema and local collection of lymphocytes round blood vessels. Section shows brightly coloured (brown) subcutaneous collagen, the cross striations of the striped muscle fibres'.

Diagnosis

Gross mental defect, aphasia, normal tendon reflexes, evidence of increased tone in the adductors of the thigh on suspension, normal electrical reactions and normal muscle structure on biopsy excludes amyotonia congenita. Marked hypotonia in the neck, arms and to some extent in the legs, gross mental defect and aphasia go against the diagnosis of congenital cerebellar ataxia and the same features differentiate it from congenital chorea in spite of the presence of choreiform movements in the hands and feet, which have been described in cases of congenital atonic diplegia. Lateral skiagram of the skull excludes platybasia and Arnold-Chiari syndrome.

All the features of the case correspond to those of congenital atonic diplegia as described by Ford (*loc. cit.*).

Comments

Air-encephalogram, though not conclusive because of the small amount of air injected (50 cc.), showed cerebellar atrophy or agenesis. The aetiology and pathology of congenital atonic diplegia are not known but probably there is agenesis both cerebral and cerebellar or early atrophy. In this case, microcephaly, aphasia, gross mental defect, motor weakness, increased tone in the adductors of the thigh (suspension test) indicates cerebral agenesis (or early atrophy and non-development) while marked hypotonia, inco-ordination, air-encephalogram and probably plagiocephaly point to the cerebellar component of the disorder. Evidently the case lies midway between pure cerebral diplegias and congenital cerebellar ataxias, combining features of both and as expected, all grades between the two extremes can be seen.

This is the first child of young parents. There is no history of birth trauma. Abnormal symptoms were noted soon after birth. The presence of a twin (uniovular?) who died of imperforate anus points towards prenatal and

agenetic origin. No other developmental defect was noted in this child.

Summary

A case of congenital atonic diplegia is described in one of the twins, the other having died of imperforate anus. Its aetiology, diagnosis and pathology have been discussed.

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'MYOIDEMA' AND 'MYOTATIC IRRITABILITY'

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MEDICAL practitioners have been familiar with the above physical signs since the early part of their clinical studies. The long familiarity has, perhaps, tended to breed a little indifference towards them with the result that a lack of clear idea about their definition and significance exists in the minds of many. Traditional explanations are passed down in books from year to year, and generation to generation, and I believe that time has come to re-assess their significance, in the light of our clinical experience, after over a century since their first mention in 1830.

A reference to medical books shows that some authors, Price (1937), mention the signs as synonymous and make no distinction between them. Chamberlain (1947) appears to make a distinction between them but assigns a common significance to both. Some mention one test and not the other. Others like Cabot ignore both and omit reference to either. The author believes that the signs are distinct because they differ in their technique of elicitation and the manner of manifestation, as may be seen from the following description:

Myotatic irritability.—The pectoral muscles should be kept relaxed. A quick tap with the finger over the pectoral region will result in a quick, fibrillary linear contraction of one or more of the muscular fasciculi, if the sign is positive.

Myoidema.—The forearm is semi-flexed to relax the arm muscles. The biceps is strongly pinched between the thumb and the index finger,

and the muscular belly is allowed to slip slowly between the pinching fingers. In a positive test, as soon as the belly slips out completely, an elongated palpable swelling appears in the muscle which quickly disappears. In other skeletal muscles the sign may be elicited by tapping the belly of the muscle with a patellar hammer when nodular tumour-like swelling appears at the site of tapping.

I have come to believe that myoidema and myotatic irritability have a common significance and both of them denote a living and mechanically irritable muscle. The distinction between them appears to be more quantitative rather than qualitative, depending upon the strength of the stimulus and the size of the muscle strands. Whereas myoidema could be elicited with some skill and by varying the strength of the stimulus in most of the males, myotatic irritability was sometimes difficult to be obtained in the obese and the thickly set.

My attention was particularly drawn to this matter a few years back, when after demonstration of the clinical signs to the students in the wards, followed by the traditional explanation that they suggest wasting disease, tuberculosis or avitaminosis, one student after another came up to me manifesting great discomposure at the presence of the signs in him. Both the 'fascicular' and 'nodular' contractions were observed in them on mechanical stimulation. The students were, and still are, in excellent health to this day. This incident modified my views about the significance of the signs and, on subsequent occasions while referring to them during clinical teaching, I mentioned them to be of no clinical significance.

I also remembered a game of my childhood. It consisted of biceps pinching as described in this paper, and bringing out a nodular swelling which we used to call, then, as a 'toad' or a 'frog'. In the case of a muscular boy, some strength and skill were required to bring out the 'toad' in his biceps. I was supposed by my friends to be expert in bringing out the 'toad' in boys in whom it refused to appear by the effort of others. The appearance of the 'toad' was believed to be a sign of well-developed muscle. This memory further convinced me about the purely physiological nature of 'myoidema'.

Pathogenesis.—Different interpretations have been put on these signs by different workers, as mentioned by Taylor and Chhuttani (1949). These are given below for the information of readers. Following conditions are alleged to have been indicated by these signs:—

1. Pulmonary tuberculosis: Tait (1872) regarded myoidema as significant of this condition.

2. Muscular fatigue: It was observed that myoidema was present after severe physical exertion and an epileptiform fit. Increased lactic acid was demonstrated in the blood.

3. Disturbed excitability of muscle fibres : This was attributed to a disturbance of the potassium-sodium ratio, and a raising of the

Between 5 ft. 2 in. and 5 ft. 8 in. heights, there were 40 persons and the average weight for their height groups are given in table II :—

TABLE II

	HEIGHT						
	5'-2"	5'-3"	5'-4"	5'-5"	5'-6"	5'-7"	5'-8"
Number of candidates	5	4	6	7	7	3	8
Average weight in lb...	108.6	107.5	110.5	122.7	121.7	122.0	122.2

excitability of both the sarcolemma and the muscle fibres.

4. Failing carbohydrate metabolism and lowering of blood sugar level : It was found that intravenous glucose abolished or diminished myoidema and that insulin increased the effect of the injection.

5. Wasting of muscles particularly due to lower motor neuron lesion : Peripheral neuritis was very often associated with myoidema. It was observed that myoidema was pronounced in wasting muscles, but not in those severely wasted.

6. Conditions producing vasomotor disturbance : The capillaries in these patients showed thickening, tortuosity and absence of contractility.

7. Unbalanced diet and malnutrition : Myoidema is reported to be a common finding in the poor and under-nourished class of patients.

8. Avitaminosis : Thiamin deficiency is alleged to be present in a large majority. But evidence has also been produced to show that myoidema did occur in cases showing no avitaminosis.

So it may be realized that a great difference of opinion exists among different workers about the significance of these signs.

The present work was stimulated by an article on the subject by Taylor and Chhuttani (1949) whose results would have the effect of boosting the value of these signs in the clinical field. My paper is based on a thorough examination of 53 individuals, including males and females mostly consisting of medical students. The tests have been elicited by the technique mentioned above. The results of the examination are given in table I :—

TABLE I

	Number	Myoidema positive	Myotatic irritability positive
Males ..	36	34 (94.4%)	28 (77.7%)
Females ..	17	3 (17.6%)	1 (5.8%)
TOTAL ..	53	39 (69.9%)	29 (54.7%)

Discussion

Myoidema was more commonly present in males (94.4 per cent) than in females (17.6 per cent) in the same age group (20 to 30 years). 'Myotatic irritability' also behaved similarly with a lower percentage in both sexes, viz, males 77.7 and females 5.8. On examining the negative subjects in males it was observed that they were flabby, fatty or plethoric and did not take exercise. The predominantly negative tests in females tend to confirm our presumption for the non-appearance of the test. The remarkably high percentage of the negative tests in the females also suggests a hormonal factor in influencing the irritability of the muscles. As all the candidates for the tests came from educated and well-to-do families, avitaminosis and malnutrition may be excluded as factors in the positive tests, beyond all doubt. Table II will lend a support to this statement. It was observed that the vegetarian or the non-vegetarian diet did not affect the results of the tests in any way as the results were found to be positive or negative irrespective of the diet. Healthy muscle appears to be an essential condition in the elicitation of the signs. - The tests are likely to be absent in muscles affected by myopathy.

Summary

With a view to investigating the significance of the signs 'myoidema' and 'myotatic irritability', 53 apparently healthy and well-nourished individuals, mostly medical students, were examined. 94.4 per cent males and 17.6 per cent females gave positive results for the former test and 77.7 per cent males and 5.8 per cent females responded in the positive to the latter test. Obesity and flabbiness of the muscles tend to mask the positive results in both.

Hormonal interrelation is suggested for the predominantly negative results in the females.

I have come to believe that the positive tests denote physiological function of the muscle, and the negative tests have no clinical significance.

I am indebted to Drs. B. N. Vaidya and Miss S. Deshpande, and to my students Messrs. G. S. Mutalik and K. K. Pai for their help in collecting the data for

this paper. I also thank the students and members of the nursing staff who co-operated with me in carrying out the tests.

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EXPERIENCE WITH FLOICILLIN '96'

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EFFICACY of penicillin has been established in infective process caused by penicillin sensitive organisms. There are, however, some drawbacks to penicillin therapy and the main ones are:

(1) The need of repeated injections causing unnecessary pain to the patient and worry to the attendant.

(2) The instability of watery solution of penicillin, if kept for a long time, necessitating making up of fresh solution.

To obviate such difficulties various oil-base preparations have been made from time to time. Penicillin in bees-wax is one such. But it is necessary to warm up this preparation before it can be injected; effective bacteriostatic level is maintained only up to 24 hours following single injections. Other repository preparations have, therefore, been devised. Floicillin '96' is one such.

Floicillin '96' is the trade name given to a suspension of procaine penicillin 'G' in pea-nut oil containing 2 per cent (w/v) aluminum monostearate. Procaine penicillin 'G' is an amine salt of penicillin and is only sparingly soluble in water. Aluminum monostearate is water-repellent; hence when procaine penicillin 'G' is made up in aluminum monostearate, the resultant compound is even more water-repellent. This being so, it is only slowly absorbed by the body fluids and therefore the drug acts in the body for longer time. The preparation is put up in easily disposable ready sterilized cartridges with 3 mega units of penicillin per cartridge.

Salivar, Hedger and Brown (1948) first discovered procaine penicillin 'G'. Buckwalter

and Dickison (1948) observed that vegetable oils gelled with 2 per cent aluminum monostearate retarded absorption of certain suspensions including salts of penicillin. Thomas *et al.* (1948) studied the effect of single injections of various penicillin salts in a pea-nut medium together with 2 per cent aluminum monostearate. They found that absorption of procaine penicillin 'G' made up in aluminum monostearate was slower than that of penicillin in pea-nut oil alone or of penicillin in bees-wax and pea-nut oil together.

Robinson *et al.* (1948) found that majority of their patients had effective serum level of penicillin after 24 hours while one-third had the same level after 48 hours. Emery *et al.* (1949) estimated the serum level of penicillin following single injections. Twelve out of their fifteen patients had serum level of 0.06 units/ml. or more, and 5 of these 12 patients had the same serum level at the end of 96 hours. The present paper records the investigations on clinical trials and laboratory control following floicillin '96' therapy.

Twenty-nine cases were investigated; the response in each case was quick, clinical results being entirely satisfactory. Apart from the pain from the needle entering the body, there was no other pain or discomfort even in children, and while the preparation was found to be useful for all patients, it was particularly so for children and infants. Local or general toxic effects were not noticed in any case.

CHART A

Therapeutic efficacy of floicillin '96'

Diseases	Total cases	Number cured following one injection	Number cured following two injections at 24 hours' intervals	Number cured following three injections at 48 hours' intervals
Gonococcal urethritis	7	7
Gonococcal vulvovaginitis.	1	..	1	..
'Sore throat' of coccal origin.	8	8
Acute bronchitis ..	3	3	3	1
Cellulitis of different parts.	8	4
Pneumonia (lobar)	1	..	1	..
Streptococcal septicæmia in sheep.	1	1
	29	22 (76%)	5 (17%)	2 (7%)

Case reports

Cases 1 to 7.—Seven male patients with acute gonococcal urethritis. In each case within 24

hours following one injection, organisms disappeared from discharge which in turn cleared up completely by 48 hours.

Case 8.—Girl of 8 with acute gonococcal vulvo-vaginitis. Within 24 hours following one injection, organisms disappeared from discharge. As, however, by the end of 48 hours, the discharge had not completely cleared up, a 2nd injection was given resulting in complete cure.

Cases 9 to 16.—Eight male patients with acute sore-throat caused by β haemolytic streptococcus; they had also some degree of upper respiratory infection. Complete cure followed within 24 hours in each case following single injections.

Cases 17 to 19.—Three cases including two children of acute bronchitis were cured within 24 to 48 hours by single injections.

Cases 20 to 27.—Eight cases of inflammation of soft tissues. In cases 20 to 23 the acute inflammation subsided completely in 48 hours following a single injection. The cases were :—

Case 20. Gum abscess with cellulitis of face.

Case 21. Abscess of forearm with cellulitis.

Case 22. Abscess of upper arm with cellulitis.

Case 23. Gluteal abscess.

Three cases required two injections at 48 hours' intervals.

Case 24. In a woman with marked pelvic cellulitis and profound toxæmia the fever abated within 24 hours of the first injection, but as pain persisted for 48 hours, a 2nd injection was given, ultimately leading to recovery.

Case 25. A man of 27 had whitlow of great toe. Inflammation subsided within 24 hours of 1st injection, but discharge continued till the end of 48 hours when a 2nd injection completely cured the patient.

Case 26. Man of 50 with many chronic infected ulcers. Inflammation subsided within 24 hours of 1st injection. A 2nd injection was given at the end of 48 hours in view of the chronicity of the case, resulting in cure. Followed up for three months, there was no relapse.

Case 27. This patient, a man of 27 with cellulitis of face with gross toxæmia, was given three injections. Within 24 hours of the 1st injection fever abated; by 48 hours inflammation was less. But as clinical condition had not improved as much as expected a 2nd injection was given. By 96 hours following 1st injection inflammation completely subsided but in view of the grave toxæmia at the onset it was considered advisable to give the 3rd injection, which though perhaps unnecessary must have hastened the recovery which followed.

Case 28.—A woman of 25 years, with lobar pneumonia. Within 24 hours of 1st injection, she was afebrile. By 48 hours she was apparently cured. But in view of the known nature of the infection and the experience with

antibiotics that in spite of abatement of toxæmia the pathological process continued, it was considered wise to give the 2nd injection which ultimately led to complete recovery.

Case 29.—Three sheep in a laboratory were suddenly found to be acutely ill. Two died within an hour of the discovery and the autopsy picture was that of acute streptococcal septicæmia, a diagnosis confirmed bacteriologically. Within 24 hours of the 1st injection the surviving animal stood up on its legs; at 48 hours when it started eating it was still ill; and a 2nd injection was now given. By 96 hours the animal looked normal but a 3rd injection was given for reasons similar to those given for case 28. The animal was ultimately cured.

Estimations of serum penicillin were made only in the 22 cases receiving the single injections.

Serum penicillin level

(1) *Test organism.*—The Oxford standard *Staphylococcus aureus* was used as the test organism. It was considered desirable to estimate the minimum concentration of penicillin required to inhibit growth of the test organism. A concentration of 0.02 units of penicillin/ml. of broth inhibited growth of the test organism. Thus 0.02 units of penicillin/ml. has been taken as minimum bacteriostatic level.

Before injecting the drug, the serum of each patient was tested for its natural bacteriostatic action against the test organism.

(2) *Inoculum.*—The inoculum was prepared by adding 1 ml. of 24 hours nutrient broth culture of the standard staphylococcus to 4 ml. of buffered broth pH 6.8. After mixing well, one drop of this diluted suspension was used as inoculum.

(3) *Test.*—Serum penicillin levels were determined at 1, 24, 48, 72 and 96 hours following single injections of the drug.

Felix tubes and racks were used for the test. Five tubes and a control were placed in the front row and one control tube in the back row. Serial double dilutions of the test serum were made in buffered broth of pH 6.8 in the five tubes of the front row, the concentrations of serum ranging from undiluted to 1 in 16. The control tube in the back row contained undiluted serum. One drop of penicillin solution was added to the tube in the back row. One drop of inoculum was added to all the tubes. The rack was incubated for 24 hours at 37°C.

(4) *Reading of results.*—Provided the control tubes showed growth, the results were read by noting the highest dilution of the serum, which inhibited the growth of the test organism.

Penicillin content was then calculated as in example below :—

If a dilution of $\frac{1}{4}$ was the highest dilution of the serum which inhibited the growth of the test organism, then this dilution contained 0.02

units of penicillin/ml. (*vide supra*); hence the undiluted serum contained 0.08 units/ml. This method of estimation is a modification of the original technique devised in this laboratory by Hayes (1944).

CHART B

Estimation of serum penicillin level in 22 cases following single injection of 1 cc. (200,000 units) of floicillin '96'

Case number	Normal	Penicillin in units/ml. of serum at different hours after single injection				
		1	24	48	72	96
1	0	0.08	0.08	0.04	0.01	0.02
2	0	0.08	0.04	0.04	0.02	0.02
3	0	0.08	0.08	0.04	0.01	0.04
4	0	0.08	0.04	0.04	0.01	0.02
5	0	0.08	0.08	0.01	0.02	0.02
6	0	0.08	0.04	0.01	0.01	0.02
7	0	0.08	0.08	0.04	0.01	0.02
8	0	0.08	0.08	0.04	0.02	0.02
9	0	0.08	0.04	0.04	0.02	0.02
10	0	0.08	0.08	0.04	0.01	0.01
11	0	0.08	0.04	0.04	0.02	0.02
12	0	0.08	0.04	0.04	0.02	0.02
13	0	0.08	0.04	0.04	0.02	0.02
14	0	0.08	0.04	0.04	0.01	0.04
15	0	0.08	0.04	0.08	0.04	0.04
16	0	0.08	0.02	0.08	0.04	0.04
17	0	0.08	0.04	0.04	0.04	0.02
18	0	0.08	0.04	0.08	0.04	0.01
19	0	0.08	0.04	0.04	0.04	0.02
20	0	0.08	0.04	0.04	0.02	0.04
21	0	0.08	0.04	0.02	0.04	0.01
22	0	0.08	0.04	0.04	0.02	0.02
Mean ..	0	0.08	0.04	0.04	0.04	0.02
Number falling below mean.	0	0	1	1	9	0

The growth of the standard strain of staphylococcus which was used as inoculum for the above estimation was completely inhibited by 0.02 units of penicillin per ml. of broth.

Discussion

The claim by the manufacturers that one injection maintains effective bacteriostatic concentration of penicillin in the blood for 96 hours is borne out. It would appear that certain diseases such as common cold, simple abscess, gonorrhoea and other milder diseases can be cured by one injection. In diseases like pneumonia or meningitis where the illness may be expected to be prolonged either from its very nature or from associated complications the injection should be repeated every 48 hours till complete recovery. It is apparent from chart B that in about half the cases, following single injections of floicillin

'96', the serum concentration of penicillin tends to fall to minimum bacteriostatic level (0.02 units/ml.) by 72 hours. Hence for greater safety injections every 48 hours are recommended in complicated cases.

In addition to specific therapy by this form of penicillin all usual ancillary lines of treatment were enforced. This included rest, diet, suitable surgical dressings, hypnotics, etc., and it is not claimed that penicillin by itself will cure all cases. The sustaining of a patient is necessary during the acute phase of invasion and if, during the time when the patient is thus sustained, the invading bacteria are killed, a cure will result. If, however, the invasion has been heavy or the patient's general condition very debilitated, it becomes necessary to support him for a longer period or more vigorously giving the penicillin a chance to deal with the organisms. For penicillin to be effective, it takes at least 48 hours to produce complete sterility of the blood stream. This aspect of treatment is apt to be forgotten in the enthusiasm of a newer drug that is undoubtedly very potent.

For administration the skin is sterilized in the usual way and then the needle is pushed into the upper and outer third of gluteus maximus muscle. Before pushing in the penicillin it should be ascertained that the needle is not inside any blood vessel. The drug should never be injected intravenously. The injection has already been mentioned to be practically painless, but it is advisable not to use the same site frequently.

Summary

Therapeutic efficacy of floicillin '96' has been tested in 29 cases.

Minor disorders can be cured with one injection while maladies of serious nature might require repeated injections at 48 hours' intervals.

Serum levels of penicillin following single injection of floicillin '96' have been followed up in 22 cases. Minimum effective bacteriostatic level (0.02 units/ml. of serum) has been maintained for 96 hours in all the cases.

We are indebted to Messrs. Infa Ltd., Bombay, for the supply of the drug to Brigadier S. Narain, Director of Research, Armed Forces Medical Service for encouragement, and to Brigadier B. M. Rao, Commandant, Armed Forces Medical College, for permission to send this communication.

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CHEMOTHERAPY OF CHOLERA WITH A NEW SULPHONE COMPOUND

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THE development of new chemotherapeutic drugs for the control of infectious diseases of intestines gives much hope and promise to the medical profession. Formo-Cibazol (Ciba) is one of them. The value of this drug in cholera deserves further investigation and study. The results obtained so far, by us, are encouraging and worthy of record. We do admit that the number of cases treated is small and the result evaluated is open to question.

Cholera broke out in this town in an epidemic form and raged from 4th August, 1949 to 9th February, 1950. Nearly all the surrounding villages were also infected.

Nearly every case of cholera in the town was compulsorily removed by the health staff to the local municipal hospital where arrangements were made to segregate and treat them. Patients from the villages also were admitted. Out of the 118 cases admitted and treated, 49 died, bringing a high case mortality figure to 41.5 per cent.

Of the villages affected, Oodiyandaram is one worth mentioning. This is about 2 miles away from the town and does not come under the supervision of the municipality. Forty-three patients from this village came to us for treatment. 10 per cent of these were in an early stage, 70 per cent in secondary and the remaining 20 per cent in late stages.

In the way of treatment we gave 25 tablets of Formo-Cibazol to every adult patient, the first 8 tablets to be taken immediately one after another or in a powder form mixed with a little honey and thereafter 2 tablets every hour. The tablets were continued in case the patient did not show signs of improvement. It was only in 2 cases we had to administer 30 tablets each.

We directed the patients to take orally large quantities of fluid which consisted of juice of 2 fresh limes, about 3 to 4 ounces of dextrose or glucose and two heaped teaspoonfuls of common

salt in a pint of cold or iced water. This mixture by mouth was intended to replace in a way, the fluid and sodium chloride already depleted from the system in watery motions and vomitings, though of course we know for certain that it cannot replace the intravenous hypertonic saline in dehydration.

All our patients were very poor people working in the local tanneries and living in very poor and insanitary localities.

Out of the 43 cases treated by us only 3 died. One was an old man who was far too advanced in disease and age. He died about one hour after the first dose of the powder. The 2nd was a child about 3 years old. She died about four hours after the initial treatment and the 3rd was a pregnant woman at full-term aged about 35 years. She was brought to us in a cart for admission. She died 2 days after the initial attack presumable due to cardiac thrombosis.

Among the serious cases treated, one needs special mention. That was a case of a woman aged about 25 years and pregnant. She was dehydrated and in a state of shock. Hypertonic intravenous saline was the most appropriate treatment. But as her condition was grave we did not undertake to give it. We gave her 25 tablets of Formo-Cibazol and a bottle of Coramine Adenosine (Ciba) and instructed her to take 60 drops of the latter in the lime juice saline mixture every half-hour. To our surprise she survived and was delivered about 10 days afterwards.

The outstanding features of the treatment as noticed by us were: (1) The vomiting and purging stopped in about 6 to 8 hours. (2) The patient urinated in about 10 to 12 hours. (3) The mortality was low, i.e. only 7 per cent. If we exclude the first case of the old man, it comes down to 4.65 per cent in comparison to the mortality figure of 41.5 per cent of the local municipal hospital. (4) No toxic symptoms of the drug were observed. (5) No other special treatment was given to the patients. (6) The patients were treated with maximum ease.

The results of the treatment are definitely encouraging and warrant further trials.

AUREOMYCIN IN THE TREATMENT OF TYPHOID, TYPHUS, CYSTITIS AND PERTUSSIS

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AUREOMYCIN is one of the new antibiotics available for use in therapeutics. It was discovered in 1947 by Duggar and his associates of the Lederle Laboratories, U.S.A. It is obtained

from the mould *Streptomyces aureofaciens* as aureomycin hydrochloride, a yellow crystalline powder. The recommended dose is 50 to 100 mg. per kilo of body weight per day for oral administration. The Lederle Laboratories have put up this drug in capsules, each capsule containing 250 mg. of the powder. This antibiotic has been tried in a wide variety of bacterial, rickettsial and virus infections and although the reports are somewhat conflicting in certain cases, it appears to be effective against certain Gram-positive and Gram-negative bacterial organisms as well as to be highly specific against all rickettsial infections. Through the courtesy of the Lederle Laboratories we received five bottles of fifty capsules each of this drug for trial in typhus and other febrile conditions. During 1949 the drug was tried in two cases of *typhoid fever*, three cases of *scrub typhus*, two cases of *cystitis* and two cases of *pertussis*. These cases were diagnosed on clinical grounds and confirmed by laboratory findings and the isolation of the causal agents, excepting those of *pertussis*. The results obtained are detailed below:—

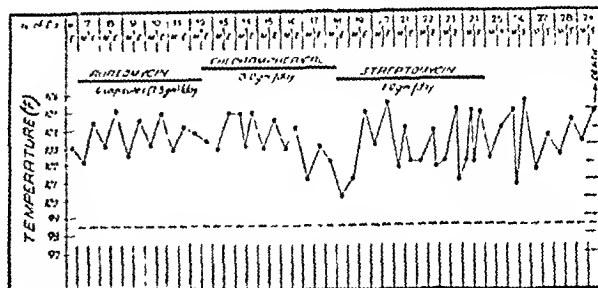
Typhoid case 1.—P. C., male, aged 22 years, weight 136 lb., admitted on 31st May, 1949, with a history of continuous fever for 6 days. On admission he was moderately toxæmic, complained of intense headache and dysuria. Temperature was 103°F. P./R. 120/26, B.P. 126/60. Tongue was thickly coated and its margin red. Blood culture was positive for *S. typhi*. The other laboratory findings were—

Hb.	.. 15.9 gm. per cent
Cell volume	.. 42 per cent
W.B.C.	.. 4,800 c.mm.
Poly.	.. 52 per cent
Lympho.	.. 42 per cent
Mono.	.. 4 per cent
Eosino.	.. 2 per cent
Plasma protein	.. 6.5 gm. per cent
Plasma volume	.. 2,350 ml.
Blood volume	.. 3,991 ml.

On 1st June, 1949, aureomycin treatment was started. On the 1st day he was given in all 8 capsules of 0.25 gm. each in divided doses, every 4 hours. On the 2nd, 3rd, 4th and 5th days he received 6 capsules per day. Aureomycin was stopped after that.

The clinical condition of the patient remained practically unchanged during the course of treatment. On 6th June, 1949, his general condition deteriorated and he passed into the typhoid state. He was stuporous and delirious. Diarrhoea now set in with marked abdominal distension and retention of urine. Temperature was high, ranging between 103°F. and 104°F. As no feeds could be given by mouth the drug was discontinued. Chloramphenical (3.0 gm. a day)

was then given by nasal tube for the subsequent 6 days and streptomycin for further 7 days (1 gm. a day) without any beneficial effect. The diarrhoea stopped soon after withdrawing



Typhoid case 1.

aureomycin, but the abdominal distension persisted throughout the illness. Towards the end, the patient developed marked signs of meningismus. The cerebrospinal fluid was however clear and sterile. The patient died of toxæmia on 23rd June, 1949, after 29 days of continuous temperature.

The case was a severe one. Aureomycin was started on the 8th day of illness and continued for 5 days. A total of 8 gm. of the drug was administered. It failed to produce any favourable effect.

Typhoid case 2.—K. D., male, aged 40 years, weight 140 lb., admitted on 1st June, 1949, with a history of fever for about a week. On admission the temperature was 104°F. The patient was moderately toxæmic, complained of headache and pain all over the body specially in the legs. Tongue was heavily coated, liver was palpable and slightly tender and there were signs of bronchitis. He was constipated. Blood culture was positive for *S. typhi*. The other laboratory findings were as follows:—

Hb.	.. 14.4 gm.
Cell volume	.. 47 per cent
W.B.C.	.. 6,200 c.mm.
Poly.	.. 72 per cent
Lympho.	.. 26 per cent
Mono.	.. 2 per cent
Eosino.	.. 0 per cent
Plasma protein	.. 6.1 gm. per cent
Plasma volume	.. 2,206 ml.
Blood volume	.. 4,162 ml.

On the day of admission, i.e. on the 7th day of illness, aureomycin treatment was started. On the 1st day he received 8 capsules of 0.25 gm. each in divided doses at 4-hourly intervals. On the 2nd and subsequent days he received 6 capsules a day. After 24 hours of commencement of treatment the only noticeable improvement in the patient's condition was a slight fall in

after that. The effect on both these cases was most striking.

Pertussis.—Bell *et al.* (1949) have recorded successful treatment of pertussis with aureomycin. In the two cases treated by us, it checked the severity of the paroxysms and improved the general condition strikingly. Though some cough persisted for about two weeks after completion of treatment, it was not distressing. Since there are very few effective drugs for the treatment of whooping cough, it is felt that aureomycin is worthy of trial. Though it cannot be considered a specific, it certainly reduces the distress and suffering. Earlier it is given better the result. In case 2 in which it was given early the result was more striking than in case 1 in which it was given after the 2nd week of illness.

Conclusion

Our observations relate only to a few cases but since the results have been quite striking in some we feel justified in recording them here :—

The value of aureomycin in typhoid seems to be doubtful. In the two cases in which it was tried, it did not do any good.

Aureomycin appears to be a very valuable and effective drug for the treatment of scrub typhus. All the three cases treated were rapidly cured and the benefit was dramatic. Aureomycin definitely brings down the temperature in scrub typhus cases to normal within a day or two though it does not benefit the other symptoms as rapidly. It definitely cuts short the total period of illness.

Aureomycin appears to effect a rapid and complete cure of cystitis due to *B. coli* and *S. enteritidis*. As seen in two cases relapses do not occur after treatment with this drug.

Aureomycin appears to be of value in the treatment of pertussis. As seen in 2 cases it reduces the severity of attacks and the duration of illness.

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A Mirror of Hospital Practice

MEDIASTINAL LYMPHOSARCOMA IN A CHILD

A CASE REPORT

By A. B. MUKERJEE, M.D., M.R.C.P.

(From the Department of Medicine, Calcutta National Medical Institute)

Introduction

IN course of a collective review of mediastinal tumours and cysts, Thompson (1947) stated that of the different varieties of tumours recorded in the literature lymphosarcomas were fairly common. Heuer and Andrus (1940) found 18 cases out of a total of 145 mediastinal tumours and these were said to arise from mediastinal lymph glands or the thymus. Twenty-nine cases out of the series were Hodgkin's disease. Haagensen (1932) discussed these tumours and described small round cell lymphosarcoma (malignant lymphocytoma) as rare and as occurring in thymic area with wide metastases. Large-celled type was regarded as more frequent, both thymus and lymph nodes being sites of origin. Age incidence according to Haagensen was between 20 and 30 years for the large-celled type and infancy for the small-celled one. Thompson (1949) says that small-celled lymphosarcoma occurs clinically, as a rule, in infants and young children. These lymphocytomas are moderately large tumours arising in the anterior mediastinum, extending up and through the mediastinum, surrounding mediastinal structures, invading the organs and metastasizing distally.

The total number of cases of mediastinal tumours recorded in children is, however, not very high and as such the particulars of a mediastinal malignancy observed in a child recently are submitted herewith.

Case notes

Complaint.—A. Ali, a Muslim male child, *at.* 2 years 6 months, was admitted into the hospital on 16th March, 1949, with the following complaints :



Fig. 1.



Fig. 3.



Fig. 2.

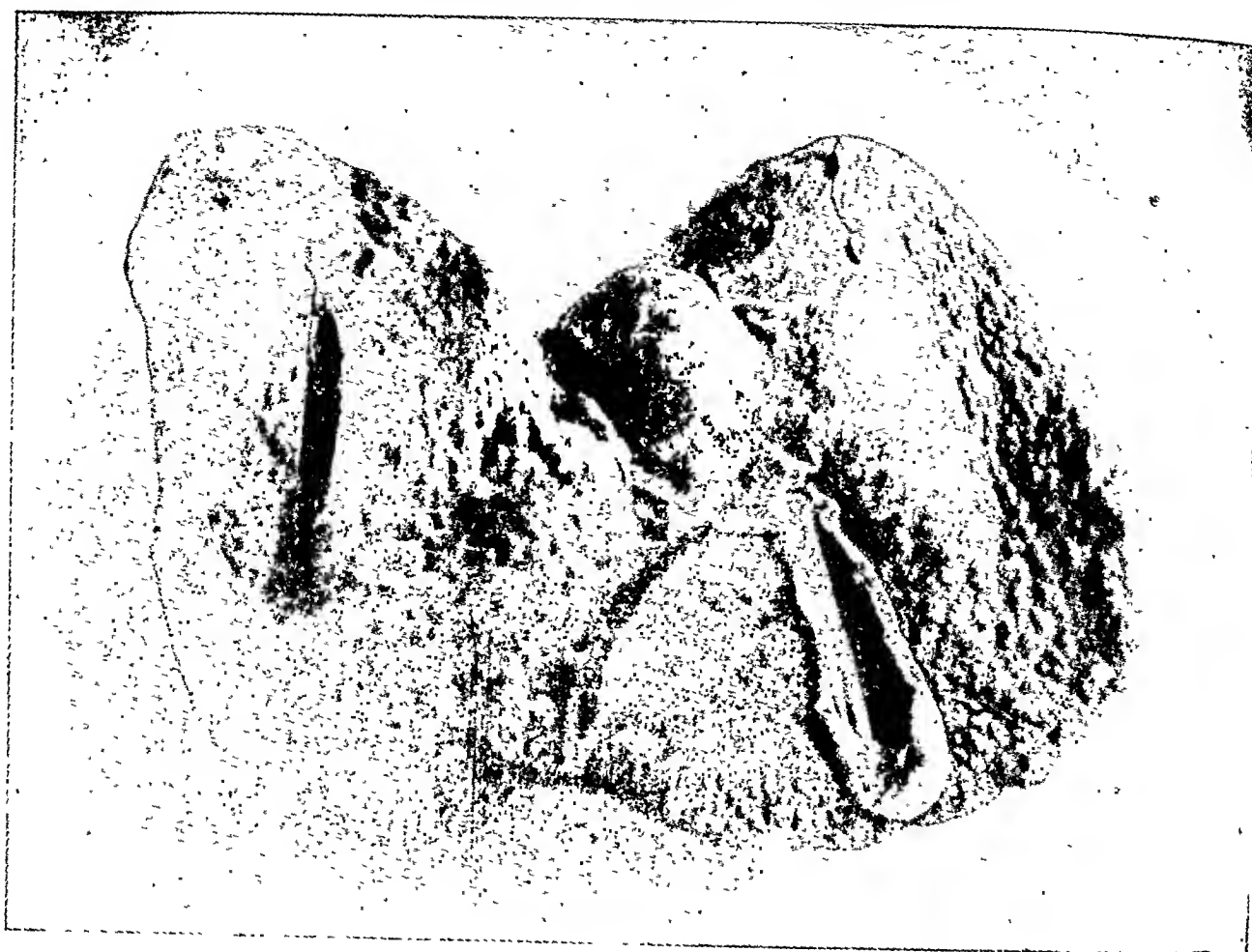


Fig. 1.—Photograph of liver showing the nodular appearance.

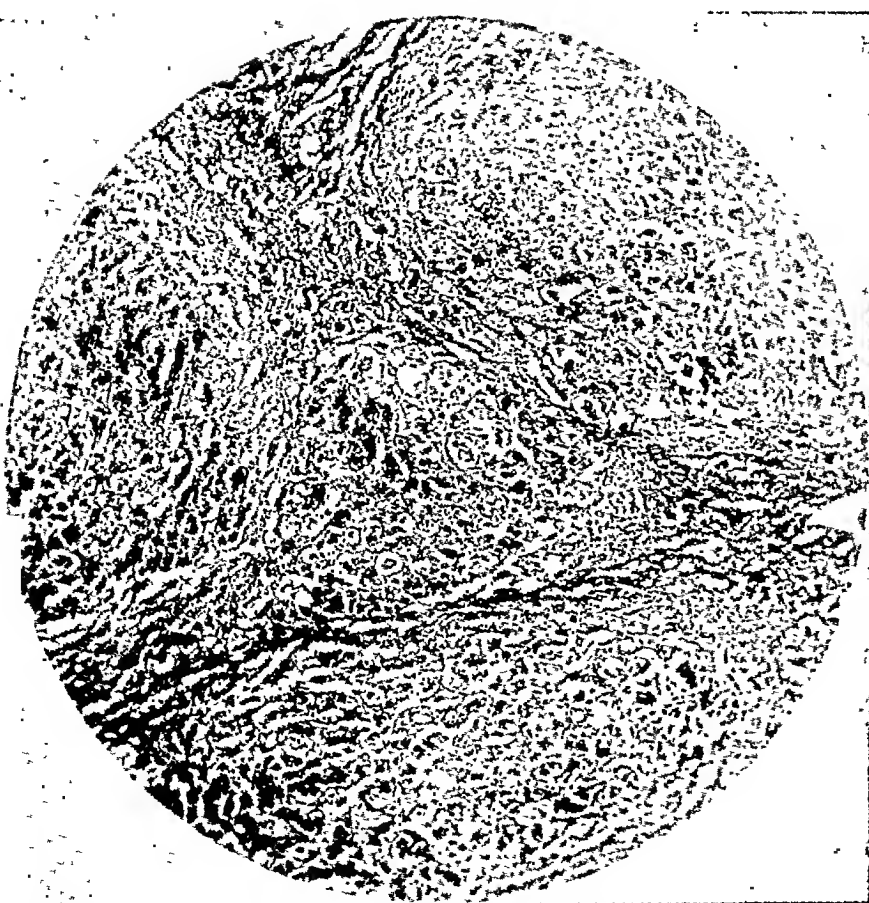


Fig. 2.—Photomicrograph of section from liver. Note the necrosis and multilobular distribution of the fibrous tissue.



Fig. 3.—Photomicrograph of a piece of liver tissue showing proliferation of bile capillaries.



Fig. 1.



Fig. 3.



Fig. 2.



Fig. 4.

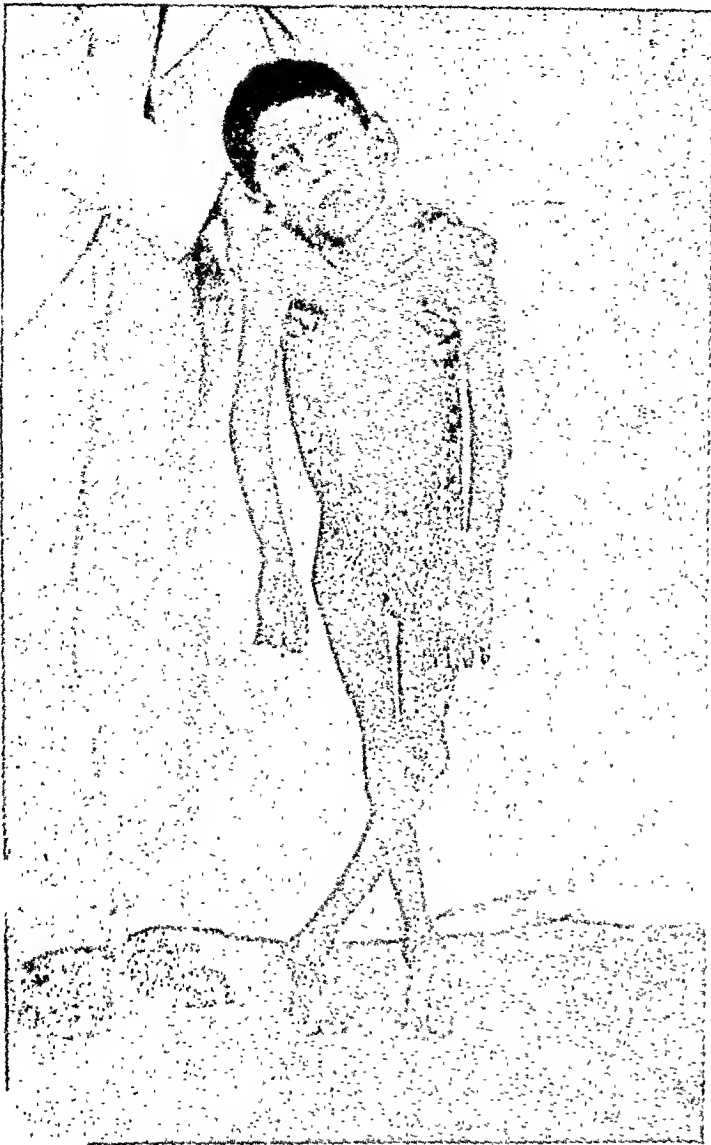


Fig. 5.

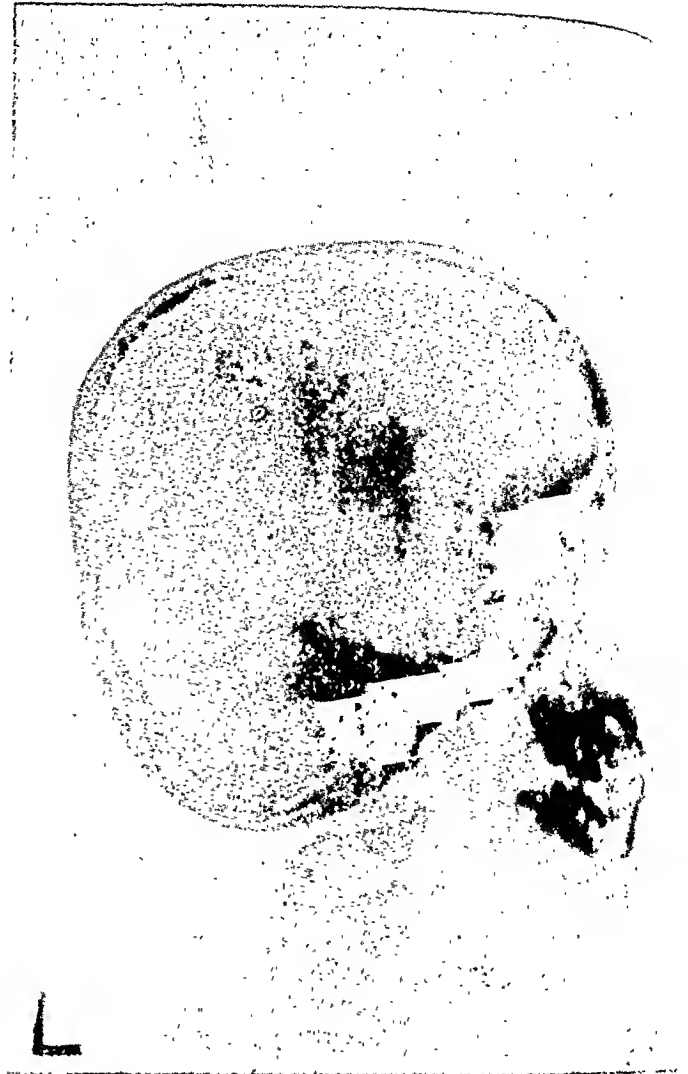


Fig. 7.—(Laterally inverted.)

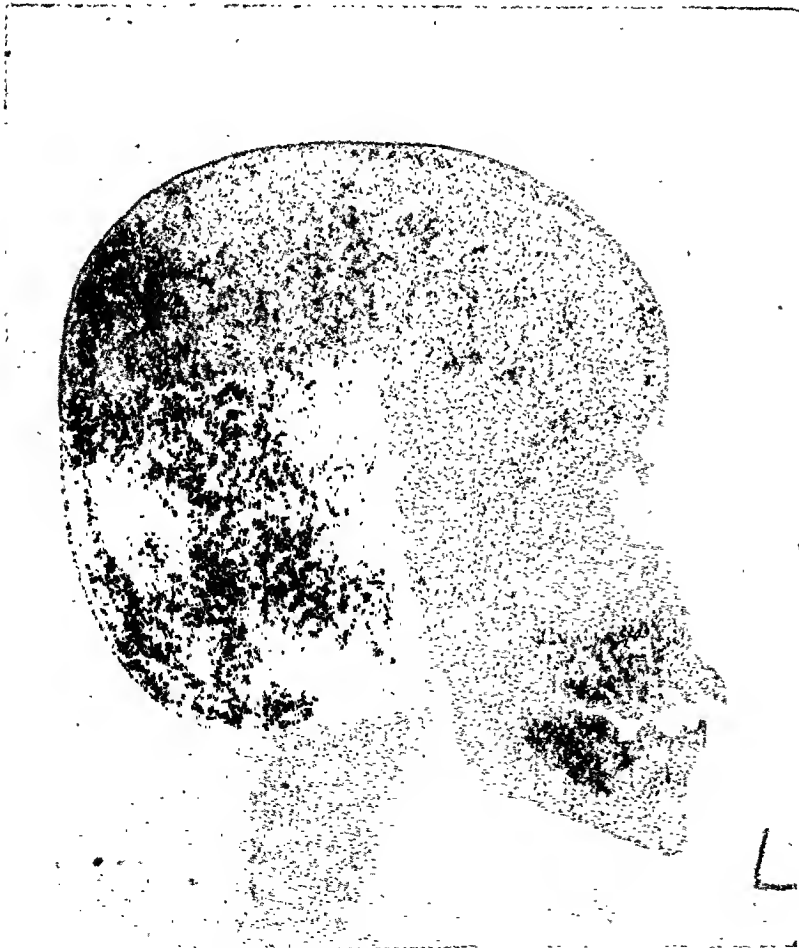


Fig. 6.—(Laterally inverted.)

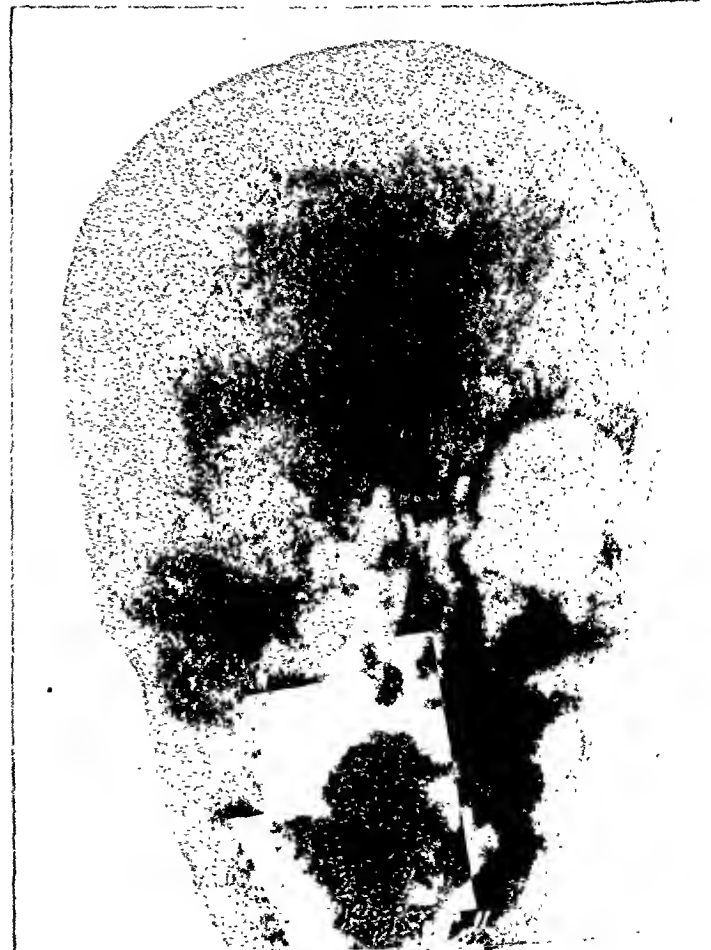


Fig. 8.



Fig. 1.

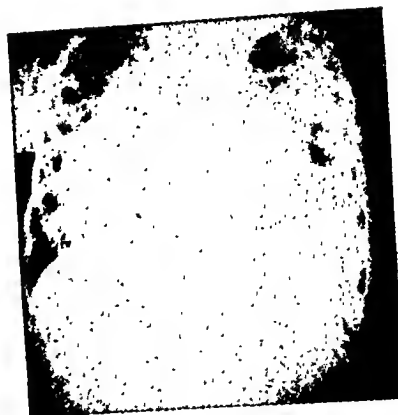


Fig. 2.



Fig. 3.



Fig. 4.

- (1) Irregular, intermittent fever, for 3 months.
- (2) Cough with scanty expectoration, for 3 months.
- (3) Progressive difficulty in breathing, for 3 months.

At the beginning the child had daily rise of temperature in the evening ushered in with chill. The temperature used to come down in the morning. There was slight cough and pain left chest with the fever at the beginning. A clinical diagnosis of pneumonia was made outside and treatment done accordingly. After 3 weeks the temperature became irregular and intermittent but the child became increasingly distressed and run down, respiratory embarrassment being the main feature.

Past history revealed nothing particular except that the child was sickly all along and was still being fed on breasts beside the usual diet.

On examination.—The child appeared rachitic with considerable wasting as seen in figure 1, plate XXXV. He was ill at ease and orthopnoic. There was moderate anemia and slight cyanosis. Neck-veins were engorged and cervical lymph nodes just palpable.

There was marked suction of intercostal spaces and the upper abdomen during inspiration. Veins on anterior chest and abdomen were somewhat prominent. The præcordium appeared bulging.

Cardiac impulse was displaced to outside the right anterior axillary line.

Left chest wall was dull throughout on percussion except in the infra-clavicular region and breath-sounds were absent generally. On the right breath-sounds were harsh and scattered. Râles and rhonchi were audible both on the right side as well as left sub-apical region.

Heart sounds were inaudible over the præcordium except in the pulmonary area where the second sound was accentuated. They were heard on the right.

Liver was palpable for about 2 fingers below costal margin and the spleen just palpable.

Temperature normal. Pulse/resp. 120/50.

Laboratory examination.—Hb. 70 per cent (Sahli), R.B.C. 3,700,000/c.mm., W.B.C. 13,200/c.mm., poly neutro 66 per cent, lympho 28 per cent, large mono 2 per cent, eosino 4 per cent.

Urine no abnormality.

Progress of the case.—On 19th March, cyanosis and dyspnoea were increasing. Fluoroscopic examination of the chest showed complete opacity of the left chest with the heart and mediastinum considerably displaced towards the right.

An exploratory puncture was made when hæmorrhagic fluid came out. In view of the respiratory distress as well as cardiac embarrassment about 235 cc. of the pleural fluid were drawn from the left side and a little air

introduced. The child got some relief and was more comfortable.

Pleural fluid was found highly albuminous and showed a large number of lymphocytes on centrifuging.

On 23rd March, a second fluoroscopic examination was done and no change was detected in the position of the heart and other mediastinal structures. A skiagram was taken as shown in figure 2, plate XXXV. It showed a large opacity extending from the root of the neck down to the diaphragm continuous with the cardiac shadow (displaced to the right) and across the upper and middle zones of the left lung, the lower left chest still showing evidence of fluid with a little air on the top.

Further laboratory examination.—Coagulation time of blood 3 minutes 15 seconds and bleeding time 4 minutes.

On 1st April, it was noticed that the cervical glands were more palpable and lateral pectoral glands were enlarged (figure 3, plate XXXV).

On 4th April, one of the pectoral glands was removed for biopsy. Histological examination of the same showed the picture of a lymphosarcoma (figure 4, plate XXXV) of the small cell variety.

Deep x-ray therapy was subsequently started. A fresh blood picture during the course showed :—

Hb. 65 per cent, R.B.C. 3,420,000/c.mm., W.B.C. 6,850/c.mm.

After four exposures had been given, on 20th April, the child had a sudden cardiac failure and died before any medical relief could be given.

Discussion

The points in favour of diagnosis of a mediastinal growth in this case were the following :—

(1) Symptoms and signs of mediastinal compression, viz, progressive dyspnoea, ineffective cough, cyanosis, prominent neck-veins and veins of the chest and upper abdomen.

(2) Hæmorrhagic pleural effusion on the left.

(3) Involvement of the heart and mediastinal structures giving rise to the appearance of a large mass occupying the mediastinum and apparently infiltrating into the left lung.

(4) Metastasis later on in anterior axillary glands.

The notable features of the case were the age of the patient; the insidious onset of the clinical picture with pain left chest, cough and intermittent fever; absence of lymphocytosis which often characterizes a lymphosarcoma at least towards the later part of the disease; and the sudden death obviously as the result of pressure on the heart including the cardiac plexus of nerves as well as the vagus. The metastatic

involvement of axillary glands helped in confirming the histological diagnosis of the case.

The histological picture showed small round cells with little cytoplasm and hyperchromatic nuclei almost filling the cell-space without an increase in the reticular tissue. Absence of pleomorphism of cells distinguished such structure from that of Hodgkin's disease while absence of a typical blood picture differentiated it from leukaemia. The name 'malignant lymphocytoma' for such a structure was first suggested by Ewing (1934). Heuer and Andrus (1940) observed that roentgenological appearance of lymphocytoma and lymphosarcoma was of a sharp or diffuse mediastinal mass, while Hodgkin's was more sharply defined or lobulated. Haagensen (1932) also stated that malignant tissue of lymphatic origin frequently has irregular, hazy borders.

From the therapeutic standpoint the small round cell lymphosarcoma like lymphatic leukaemia is not very radio-sensitive but the large cell type is, Hodgkin's disease being only moderately so. According to Heuer and Andrus (1940) surgery is of no value as yet in malignant lymphocytoma and lymphosarcoma. The average course of a lymphosarcoma is possibly not more than six months.

My thanks are due to my ex-senior house physician, Dr. S. N. Roy, who helped me in having all investigations done and to Capt. S. Maitra, F.R.C.S., Principal-Superintendent, Calcutta National Medical Institute, for allowing me to report this case.

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A CASE OF ACUTE NEPHRITIS TREATED WITH AN ANTIHISTAMINE DRUG

By A. SAMAD, M.B.

and

S. C. KAPOOR, M.D. (Luck.)

RECENTLY the number of diseases coming under the ætiology of allergic reactions has shown a rapid increase and so also the number

of patients suffering from allergic diseases. One of these diseases is acute nephritis. Knowledge acquired from clinical experience and experimental work tends to show that acute nephritis or type I nephritis is due to allergic inflammatory changes in the glomerular capillaries. This experimental nephritis in animals has been successfully treated with antihistamine drugs, thus introducing a fundamentally new approach to its treatment. The following report shows the good effect of antihistamine drug in the treatment of acute nephritis.

Case history

The patient was a boy aged five years, who started with fever on 4th November, 1949. Two days later when seen by one of us, he had temperature ranging between 101°F. and 103°F. with no other signs or symptoms. Blood examination showed no malarial parasite, no leucocytosis and practically normal differential count. On the sixth day of fever his parents noticed that the child had some difficulty in passing urine as well as some puffiness of face. The quantity of urine was also markedly decreased. Urine examination showed albumin in heavy cloud with red blood cells, pus cells and epithelial cells. Culture of urine showed it to be sterile. Total W.B.C. count on that day showed a marked leucocytosis (18,600/c.mm.). He was started on 100,000 units of penicillin every four hours. On the ninth day of disease, i.e. four days after starting of penicillin, temperature was still high, and urine examination showed albumin, red blood cells, pus cells and epithelial cells. He was given Antistine (Ciba) half tablet three times a day from the next day. Within twenty-four hours his temperature came down to 99°F. It then ranged between 99°F. and 101°F. for the next three days and then was normal. Quantity of urine also increased on the fifth day after starting Antistine. Urine was completely cleared of albumin, pus cells and red blood cells. Antistine was given for seven days and then stopped. Up to the time of writing (22nd April, 1950), the child is perfectly normal with normal urine.

Discussion

Ætiology of acute nephritis has been a subject of controversy. Both infection and allergy have been blamed for it. In the above-mentioned case we gave penicillin to control any infection, as the patient showed leucocytosis. Apparently it did not help the patient as shown by the temperature and urine examination. When, however, an antihistamine drug was given, the patient showed a marked improvement. The temperature became normal and urine also cleared up. This line of treatment is worth a trial in cases of acute nephritis, as it gives a better prognosis, shortens the illness of the patient and indicates the ætiology of this disease.

Indian Medical Gazette

MAY

GERIATRIC MEDICINE

In youth I sought the golden flower
In many a wood and wold
But now I have come to the autumn hour
When all the leaves are gold.

THE leaves are the days of life of a mature observer and the gold the wisdom collected from his surroundings with the aid of judgment made mature and sound with the passage of time.

Grow old along with me,
The best is yet to be,
The last of life for which the first was made.

The verses described a man who had survived the struggle for existence in an age when the expectation of life was considerably less than it is to-day which is an unprecedented period in human history: 'An age of age is here' (Stieglitz, 1949). The pyramid of population instead of being broadest at the base, as it was in pre-World War I days, is broadest in the middle (Crew, 1948).

This change has been brought about by medical men of our time who have followed their mission of healing in and between the two wars: In the midst of death they have built a new pyramid of life. It is their responsibility and privilege to look after this new structure of the population. The branch of medicine which deals with the care of the aging and the aged is Geriatric Medicine.

Rapidity of rise in expectation of life.—While problems of feeding the increasing population of the world are engaging the attention of the politicians (and even the statesmen) enough is not being thought and said about the rise in the expectation of life. There are more elderly men and women alive to-day than ever in human history. The expectation of life rose by 10 per cent after World War I. It is bound to rise even by a higher figure when the present turmoil created by ideologists, time servers, profiteers and black marketers has subsided and medical men of learning and experience have time to make use of new life-saving and life-preserving devices.

Longevity without senility.—Such a course of life appears to be extremely likely in the light of what has been attained by sulpha drugs, antibiotics, new vitamins like B₁₂, new hormones like cortisone and devices for washing blood free of substances like urea and NPN. The

medical man will be required to be a critical observer of the first sign of senility with a view to removing, not with a view to compromising with, it. Only neglected cases will become senile. Even congenitally defective hearts of 'blue boys' and damage caused by coronary inadequacies in later life will be attended to with the same confidence which is available for appendicitis, when more tenacity of life in the flesh and less danger from infection are assured.

The tenacity of life in the flesh is a characteristic of the species at present. It is known to the experimenter who selects a rabbit for an experiment of a short duration and a cat for one of a long duration. It is also known to the callous meat-seller who cuts pieces of flesh off a live tortoise—made illegal in Calcutta 2 years ago. That 'something' which builds up this tenacity may not be beyond the scope of vitamins and hormones and is probably waiting just round the corner to be harnessed for human service. Its near relations have served already in the building of the new pyramid, by one generation of medical men. Longevity without senility should be the target of the modern medical man.

Theories of aging.—Three conceptions may be considered: (1) Involution results from exhaustion and depletion of vital reserve by work and wear. This view is favoured by the lazy. (2) Atrophies of senescence are due to disuse. This view is favoured by the restless. (3) Primary changes occur in the interstitial tissues, fibres and fluids surrounding the essential cells. These changes are comparable to what occurs in a leaf: *Pari passu* with the development of the essential structures there develops a corky layer which, later, will cut the leaf off the stem and seal the raw surface on the stem. With such changes in the human body cortisone or even ACTH should be able to deal. They have recently cured all collagen diseases dramatically (Kersley, 1950; Editorial, 1950a, b).

Certain prosaic items.—Before prints from the rosy picture painted by the aid of recent advances and future expectations in medicine become generally available, certain items specially applicable to the aging and the aged merit mentioning. They are: (1) Mental changes with normal aging. Slow cerebration, or difficulty in selecting an idea or a memory, is commonly believed to be the usual failing. It is not free from fallacy. The brilliancy of the young is largely due to a paucity of ideas and memories; they have so few items stored in their mentality that there is little difficulty in storing a new one or sorting out an old one (Todd, 1946). 'Every old man knows what it is to be young and foolish but not a single young man knows what it is to be old and wise'. (2) Morbid mental changes of senility. Essentially they are (i) Involutional Melancholia, (ii) Senile Psychosis, and (iii) Arteriosclerotic Psychosis. In general, the prognosis of morbid

mental processes of later life is not good (Overholser, 1949). Much, however, can be done to make the patient and the family happy, specially if the disease is detected early. (3) Digestive processes. They are defective from several causes and aim at reducing intake which is not a disadvantage altogether. If nutrition is suffering specially prepared food may be prescribed. Avitaminosis should not be allowed to occur. (4) Exercise. Some form of exercise is always possible. There is no special merit in hard exercise which after all is undertaken by men of means to copy the life of a manual labourer, for a change. The Alpine climbers undertake occasionally what the labourers of the locality are doing daily. The local porters accompanying the Everest climbers do much more. Players of hard games should give them up in middle age and take to what they can keep up in old age. If nothing else is possible massaging should be substituted for the ordinary forms of exercise. One can massage one's own body while taking a bath, with the lubricant action of soap. Breath should not be held: Mouth should be open during exercise (Todd, *loc. cit.*). (5) Skin and hair. They need attention. Protection against the weather, and comfortable clothes and shoes will suffice in most cases. Special medication and devices for varicose ulcers may be necessary. (6) Sleep. A moderate degree of fatigue and a good digestion should be ensured. Flatulence should not be allowed to occur. Sleeping draughts will be required in some cases only. (7) Constipation. The 'inner cleanliness' is not necessary. No laxative can possibly be harmless. Food should be so selected that a daily evacuation results. (8) Cardiovascular system. To reach real old age the cardiovascular system must be sound (East, 1946). Only discomfort after food, specially distension after a heavy dinner at night should be avoided. It embarrasses the coronary circulation. Many old men of position and means die unexpectedly after annual dinners of clubs, societies, associations, companies, lodges and services. (9) A man is not really as old as his arteries. Capillaries are more important than arteries: Most of them can be kept in good order with a brisk rubbing with a towel, after a bath. (10) Emphysema. Attention to the upper part of the nasopharynx and mal-digestion will correct much breathlessness in spite of the changes in the chest wall (Todd, *loc. cit.*). Pneumonia lost its terror for the old many years ago. (11) Care of the feet. This applies almost solely to the feet in European shoes. Such shoes for old people should be made, not bought. The fit should be comfortable. (12) Endocrine dysfunction. The pituitary, thyroid and adrenals are usually decreased in size in old age (Davis, 1949). The deficiency may be made good judiciously. The new hormone cortisone may help. (13) 'Rheumatics'. They have been the bane of the aged in colder climates. The new hormone is likely to eliminate them al-

together. They are not much of a problem in India. Apart from the climate, one is to give credit to the Indian diet also. (14) Genito-urinary tract. The benign enlargement of the prostate appears to be amenable to testosterone (Todd, *loc. cit.*). A careful examination, however, is necessary to exclude serious trouble and surgical intervention. The discomforts of menopause are temporary and should be endured. The need for surgical intervention should again be excluded. (15) Pseudofractures. These x-ray appearances, due to loss of calcium cross-section wise, do not appear to cause much inconvenience. They are important medically—in an elderly person after an accident or an act of violence they may be mistaken for true fractures. (16) Aging the young. Apart from making the ape look pathetic this effort serves no useful purpose. It may on the other hand do serious harm. Wearing nether garments with a belt (or other devices which compress the abdomen) instead of with braces may upset digestion or even circulation in a well-nourished (= overnourished) elderly man. The 'new look' may do the same to an elderly woman. Dyeing of the hair may cause serious skin trouble. Even perpetual consciousness of the artefact and the fear of possible imperfection in certain areas may be trying to the consciousness. Excessive facial massage converts skin into hide with the passage of time. The aim should be to grow old gracefully. Mature age has its own interests in addition to those of early life which can be preserved 100 per cent by living a 100 per cent natural life:

My heart leaps up when I behold
A rainbow in the sky.

The opposite effect is produced not by old age but by unnatural living:

I have lost the sunshine and the roses,
I have lost the heavens so blue,
I have lost the beautiful rainbow,
I have lost the morning dew.

(17) 'Second sight', etc. The continuous growth of the crystalline lens of the eye (an instance of a structure which does not cease to grow) leads to an increase in its density and refractive index, curing some subjects of presbyopia. Such subjects can read without glasses again. This fact should not be allowed to encourage the old to attempt other pursuits of youthful subjects. Even another set of teeth sometimes erupts—instances appear to be commoner in India than elsewhere. The teeth interfere with dentures. (18) Weight and age. The latest finding, from the life insurance records, is that an allowance for over-weight for age after 25 is not justified (Carlson, 1949). The intake of food must be reduced in over-nourished subjects. The Oriental conception of a ration granted for a life [*Dána pāni* = foodgrain (and) water] is useful for explaining the reduction in food. One may finish one's ration in 'three score and ten' years (the optimal Western

limit) or in 'one hundred and twenty-five' years (the optimal limit of ancient India). Probably with the aid of newer knowledge it will last even longer. (19) Libido. Requests for its improvement should be discouraged. Here it may be mentioned that an operative libido and a mere interest in the opposite sex at its best are two different propositions. The latter appears to be beneficial to the endocrine and accounts for the elderly patrons of night clubs. The same purpose may be behind an ancient temple in India. There is another instance:

'Now King David was old... his servant said unto him, Let there be sought for my lord the king a young virgin: and let her stand before the king... So they... found Abishag and brought her to the king... And the damsel was very fair... but the king knew her not.'

(20) The agony of death. This appears to be a myth. Men die very much as they fall asleep, often suddenly with a short pleasurable aura, at other times with a tiredness which resolves itself... (*loc. cit.*). Even death by hanging, when properly carried out, is not an agony as is evidenced by the placid features of the face of the body examined. Catastrophies like death from hydrophobia and tetanus may be different but can be made painless. Euthanasia is never indicated for the sick. It may be employed some day for criminals. (21) Feeling of uselessness. It should be removed by (i) social effort or (ii) legislation. The expectation of life having increased the period of usefulness has also increased but this increase has not yet been recognized by agencies providing employment. Both these items must be expanded further.

Social effort at finding employment for the aging and the aged.—In providing a new deal for the old, Birmingham has led the way (Mugliston, 1949). New homes which are really homes, new workshops for the workable and new clubs for the clubable have been provided. Two different ways have been found for employing old people: (1) They work as long as they can under normal conditions of work. The management suits the work to the worker's capacity. *The work done is of real value to the firm.* (2) A separate workshop has been built and equipped with machinery, and men too old to be employed in the big works are given jobs here.

Between a fifth and a quarter of Birmingham's 100,000 old people are employed already.

The original report from which this account of Birmingham's leadership has been abstracted was written by a journalist aged 80 and still active.

The employment of the aging and the aged in industry in India, fortunately, is not a problem yet. The factory worker has a home in the village to which he retires. The joint family system keeps him as the head of the family.

The employment of the scientific and technical workers, however, is a problem. As a matter of fact their non-employment is creating an amusing situation: Young men are going abroad, for scientific and technical education, to sit at the feet of foreign teachers who as teachers differ from Indian teachers only in being older. Indian teachers are not allowed to grow as old as their foreign opposite numbers. The system in addition to creating an evidence for racial inferiority is coming between the young men of the country and their heritage of scientific and technical knowledge which is in the keeping of mature teachers.

Legislation for the employment of the aging and aged.—If the pyramid of the population is broadening towards the upper half, the voting strength of the population in the upper half will naturally increase and they will legislate in their favour before long.

Medicolegal consideration for the aged.—Some old men commit crimes for the first time. Should they not be judged as senile delinquents to correspond to juvenile delinquents (Editorial, 1947)?

Parallelism with the central nervous system in the body.—The system is not renewable, cannot be repaired and is the oldest tissue in the body at any time. Yet it works with the younger tissues. So are the aging and the aged in the body politic for which the Prime Minister fixed the retiring age at 70, the other day. If involution can be controlled it may be even raised with safety. A place should also be available for the aging and the aged in ordinary everyday life.

Age, the alpha and the omega.—Life on earth became possible when the planet lost much of its radio-activity through growing old. Such was the alpha of life. The shape of the pyramid of the population to-day suggests that the final destiny of the human race on the planet is also going to be controlled by the aged. Such will be the omega of life. Hence the need for the care of the aging and the aged: Geriatric Medicine: the alpha and the omega of this account also.

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Medical News

LEPROSY TRAINING COURSE

(Copy of Circular No. 37/L, dated 29th May, 1950, from the Honorary Secretary, Hind Kusht Nivaran Sangh to all State Branches)

It is proposed to hold the next Leprosy Training Course at the School of Tropical Medicine, Calcutta, from 16th August to 16th September, 1950, both days inclusive, provided sufficient number of candidates is forthcoming. The selection of candidates will be made by Dr. Dharmendra, Officer in charge, Leprosy Research Department, School of Tropical Medicine, Calcutta. It is therefore requested that names of candidates may be submitted direct to him on the enclosed application form which should reach him by the 15th July, 1950.

The value of the course would be greatly enhanced if officers of the senior grade are sent up for training. It is therefore requested that doctors of the senior grade, who have special aptitude for leprosy work, should be nominated. A copy of the syllabus for the course is enclosed for your information.

No registration fee will be charged from candidates attending the course. Their travelling expenses should, as usual, be met either by the State Branches concerned or by the doctors themselves or their employers.

Application for admission for a Special Leprosy Training Course to be held from 16th August to 16th September, 1950, at the School of Tropical Medicine, Calcutta

1. Name, age, qualifications.
2. Name of medical college or school from which qualified.
3. Date of qualifying
4. Past posts held by applicant.
5. Present post held by applicant.
6. Past experience in leprosy work.
7. What facilities will he have for anti-leprosy work after taking the training?
8. Expenses to be borne by.
9. Permanent address.

Syllabus for the Leprosy Training Course held under the auspices of Hind Kusht Nivaran Sangh (Indian Leprosy Association) at the School of Tropical Medicine, Calcutta

1. LECTURES

A course of 20 lectures covering the aetiology, clinical manifestations, classification, diagnosis, differential diagnosis, course, pathology, bacteriology, epidemiology, treatment and control of leprosy.

2. DEMONSTRATIONS

The demonstrations will cover the following subjects: clinical examination, case charting, bacteriological examination, diagnosis, diagnosis and method of treatment.

Histopathology, the lepromin test, methods of vey and chemistry of the preparations used in the treatment.

3. PRACTICAL WORK

Clinical and bacteriological examination of case case charting, treatment.

4. TUTORIAL CLASSES

5. EXAMINATION

At the end of the course a practical and theoretical examination will be held, and certificates will be given to the successful candidates.

SOAPLESS 'SOAP' TO DISSOLVE THE INSOLUBLE. 'RADIOSONDE' RECORDS TEMPERATURE AND HUMIDITY OF UPPER AIR. SCIENTIFIC RESEARCH IN MANY FIELDS

(Reproduced from a release dated 6th April, 1950, issued by Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta)

A NUMBER of chemicals—washing nuts, for example—possess typical properties of soap without in any way being chemically related to ordinary soaps. These newer detergents have of late assumed industrial importance and their prices have been brought down to fairly competitive levels.

A special property of these detergents is their power of dissolving an otherwise insoluble substance. This phenomenon is called solubilization. For example, they can make oil mix with water to a perfectly clear solution. Research to discover how much water dissolves in oil and other organic solvents by use of a definite quantity of a detergent is being carried out by the Indian Association for the Study of Soapless Detergents in Calcutta.

The Association is also investigating the use of preparing cellulose acetate, an important material in commerce and one that is used extensively in lacquer, plastics and rayon, in good yield and of good quality from Indian cotton.

The process, in short, consists of treating cotton with sulphuric acid, glacial acetic acid and acetic anhydride to obtain what is technically called a primary acetate. This is subsequently transformed into the secondary cellulose acetate of commerce by adding regulated quantities of water to acetylating bath. Comparison of products at every stage with similar products obtained from Egyptian cotton has shown that it is possible to obtain good quality cellulose acetate from medium staple Indian cotton by a rather easy process.

QUICK FINDING OF PLANE'S CENTRE OF GRAVITY

Details of some other lines of scientific research being conducted under the aegis of various Ministries of the Government of India and their research organizations follow.

A portable electric instrument for rapid determination of the position of the centre of gravity of Viking Mk. IB. Aircraft, for any load distribution, has been developed in the research and development laboratory of the Civil Aviation Department. The basic principle of the instrument is applicable to other types of aircraft as well.

As far as is known, this is the first instrument of its kind ever developed and it is hoped that further development will reduce the chances of error and the amount of work by operational personnel.

Two different types of 'radiosonde' have been developed for observation of conditions of temperature and humidity in the upper levels of the atmosphere, reports the Indian Meteorological Department.

Radiosonde is a small self-recording instrument fitted with a tiny radioltransmitter which is sent up through the air, attached to a hydrogen-filled balloon. As the instrument ascends, it emits pulses from which pressure, temperature and humidity can be computed when these pulses are recorded on a suitably designed radio-receiver at ground level.

The instrument as well as the ground equipment which have been manufactured in the Departmental Workshops at Delhi and Poona, are at present being used at 10 stations in the country.

BIHAR ROCK TYPES

Interesting rock types representing different periods of intrusion and degrees of metamorphism have been observed in the Gomoh area. Detailed study of these is likely to throw much light on correlation of the basic rocks of Bihar.

The Indian School of Mines and Applied Geology in Dhanbad reports study of the following problems: Variations in chemical durability of glass with different compositions; range through which the compositions may be varied without seriously affecting durability; effects of minute impurities; associating raw materials and those derived from posts or tanks, on glass; effect of annealing on the chemical durability of glass (it has been established that annealing improves chemical durability); effect of ultra-violet radiations of both long and short wave lengths on the chemical durability of glass.

Successful attempts have been made to evolve a process for estimating simultaneously phosphorus, total chlorine and nitrogen in coal. The progress is also suitable for estimating the inorganic impurities of coal in a single operation.

PACKING OF WOOLLEN TEXTILES

The Indian Standards Institution reports development of the Indian standard code for sea-worthy packaging of woollen textiles, IS. 32 (price Re. 1). The code deals with the packing of woollen textiles intended to be conveyed by sea and describes the materials needed for packing, packing procedure for woollen cloth and yarn, marking of bales and tests for the quality of packing materials.

The method described is also applicable to bales intended for inland transport where distances are great, time spent in transit considerable, climatic conditions extreme and consignments frequently off-loaded and re-loaded.

COSMIC RADIATION

In cosmic radiation, the Tata Institute of Fundamental Research, Bombay, has undertaken a project for measurement of the intensity of radiation at high altitudes by balloons, at places of widely different magnetic latitudes. These experiments should yield valuable results regarding variation of the intensity of cosmic radiation with latitude and altitude. Cosmic ray data are received by a wireless transmitter sent up into the atmosphere.

Measurement of the intensity of cosmic radiation of high altitudes with special photographic plates is also undertaken.

SUGARCANE RESEARCH

It is learnt from the Indian Central Sugarcane Committee that with a view to improving the agricultural aspect of the sugar industry, promising seedlings and sugarcane fluff obtained from crossing different varieties are being sent to state research stations for the evolution of varieties suited to different soils and climates. Some promising varieties have been evolved and are under cultivation in various parts of the country.

In connection with the Ravalgaon sugar-candy scheme, research is being conducted on the manufacture of sugar-candy and homoeopathic sugar pills.

'JOURNAL OF SCIENTIFIC AND INDUSTRIAL RESEARCH'. ROCK SALT DEPOSITS OF MANDI

(Reproduced from a release dated 14th April, 1950, issued by Press Information Bureau, Government of India, New Delhi)

Salt deposits of Mandi constitute (after partition) the only source of rock salt in India. Urging development of the salt industry as Mandi, an article in the April issue of the 'Journal of Scientific and Industrial Research' deals with the geology of the deposits, reserves of salt in the area and quality of salt mined, and describes the three important mining centres, Guma, Darang and Maigal. It also contains suggestions for the working of these deposits.

Reserves of salt in the Mandi area are estimated at 70 million tons. If an igneous extrusive origin of these deposits be accepted, the reserves may be several times this estimate.

The average annual production of salt from Guma, Darang and Maigal is only about 100,000 maunds a year. The Guma deposits are best worked by driving bore holes and recovering saturated brine. Darang salt is inferior to Guma salt, and mining can be done only by judicious 'open' operations. In the Maigal area, where brine springs exist, 1,000 maunds of salt can be produced per day. The brine is 99 per cent pure, and could profitably be used in the manufacture of salt by solar evaporation.

The selling up of a refinery at Maigal producing 60 tons of white granular salt per day, employing a thermo-compression unit, is recommended in the article. A commercial unit costing Rs. 15 lakhs with a daily productive capacity of 60 tons should produce salt at Rs. 15 to Rs. 20 per ton. A larger plant could be erected at Joginder Nagar with brine supply from Guma.

The combined output of salt from these sources is calculated to meet the requirements of Punjab, (I) and the western districts of the U. P.

ALKALOIDS FROM HILL PLANT

Alkaloids contained in Indian *Stephanias* (*Gindaru*) are the subject of a second research paper in the Journal. Four species of *Stephania* grow abundantly at 3,000-8,000 feet in the Himalayas, Khasi Hills and other hill tracts all over the country. The acid tubers are used in indigenous medicine for the treatment of pulmonary tuberculosis, asthma, dysentery, fevers and intestinal complaints.

Examination of the tubers of the plant has resulted in the isolation of three crystalline alkaloids, which are being investigated for their chemotherapeutic properties. A number of salts of these alkaloids have been prepared and characterized.

Another research paper relates to the development of rancidity in Indian shark-liver oil and the consequent destruction of vitamin A. Methods to stabilize shark-liver oil during storage with the help of suitable antioxidants is discussed. Vitamin A in shark-liver oil is destroyed more quickly when exposed to light and subject to higher temperature storage conditions. Of the antioxidants tried, a mixture of isobutyl gallate and tartaric acid provides adequate protection for the vitamin.

Other articles in this number of the Journal relate to: Estimation of coconut oil in samples adulterated with white oil, Study of Seismology in India, and Chemical examination of depolymerized castor oil gel. The editorial deals with the question of 'Science and State aid'.

Public Health Section

THE USE OF POTASSIUM PERMANGANATE IN THE DISINFECTION OF WATER

By RADHAKRISHNA BANERJEA, M.B., B.S.,
D.T.M., D.P.H.

(From the All-India Institute of Hygiene and Public Health)

POTASSIUM permanganate is one of the agents which is used for disinfecting water in India. But on account of certain disadvantages it is not much liked. These are: it produces objectionable stains and unpleasant taste in the water, it imparts colour to the water due to reduction of permanganate by organic matter resulting in formation of brown colloidal manganese compounds, its action is not continuous and it loses oxygen rapidly in oxidizing organic matters. Moreover, it is costly to use. But it has got an important advantage and that is, it is a stable compound.

Potassium permanganate is generally used by adding the chemical to the water in such an amount which will produce some pink colour. But the practical details of its use are different in different places in India. For example, in the Central Provinces, sufficient potassium permanganate is added to well waters which will retain a slight pink colour for at least half an hour. In the Punjab sufficient permanganate is added to produce a uniform deep pink colour after thorough agitation of the water. In the United Provinces addition of permanganate is regarded as sufficient if a very faint pink colour persists after one hour. Thus, there is no uniform method followed in its use due to lack of knowledge about the effective concentration and period of contact which are necessary to kill the bacteria in well and tank waters.

In this work an attempt was made correctly to assess the efficacy of potassium permanganate as a disinfectant of well waters. It was determined: (1) How far a residual pink colour retained after various periods of time is a measure of the efficacy of the permanganate used. (2) How far effective is this chemical in killing the coliforms and how far changes in the organic matter content and pH within normal range affect such action. (3) How far effective is potassium permanganate in killing the three intestinal pathogens, namely *Vibrio cholera*, *Salm. typhi* and *Shig. flexneri*, when added to surface waters like well or tank waters.

I. Studies on the residual colour left behind after permanganation of water

(a) Use of colour chart in determining the strength of potassium permanganate in water

There is no method suitable for ascertaining in the field the strength of potassium permanganate

when added to water and specially for determining the residual colour left behind after the permanganate has acted on the water for some time. It was thought that if a simple method could be devised, it would be of great help in the disinfection of water by permanganate and will facilitate the carrying out of the present work.

With a view to meeting this want, a colour chart was prepared as follows: Different strengths of potassium permanganate in distilled water were prepared and put up to the mark in Nessler's cylinders of 50 ml. capacity having the inner diameter of 3 cm. and the 50 ml. mark at 6.5 cm. height from the bottom. The colour as seen from the top through the entire depth of the fluid was painted on a white sheet of paper. Similarly colour as seen from the side of 6 inches by $\frac{3}{4}$ inch test tubes filled with different dilutions of permanganate in distilled water was also painted. The painted chart was used for comparing the colour given by known strength of permanganate with these known colours in the chart. In filling Nessler's cylinder with the water containing permanganate in an unknown strength, an empty cylinder of the above specification was used and due care was taken to fill the water exactly up to the 50 ml. mark. When test tubes were used, size of 6 inches by $\frac{3}{4}$ inch was chosen.

Difficulty was experienced in determining the strength of permanganate in treated waters on account of yellowish and sometimes orange tint that was produced in such waters, due to production of coloured precipitates. So, before comparison of the permanganate colour, the precipitates were removed by filtration. Filtration, however, through ordinary filter papers, removed a good amount of the permanganate colour also. So, instead of filter paper, glass-wool was used for filtering.

(b) The amount of diminution in colour suffered by permanganated waters of wells and strength left behind, as determined by the colour chart

The strength of potassium permanganate recommended for disinfecting waters in India is usually 1 drachm for 200 gallons, which roughly comes to a strength of 1 in 225,000 parts. Converting this figure into round numbers, experiments were performed to see how long the colour of 1 in 200,000 strength of permanganate in well water persisted, what was the proportion of such water samples which completely discharged the colour produced by this strength of permanganate after definite periods of contact, and, when not discharged, what was the amount of diminution in colour suffered by these waters. Similar experiments were also performed with higher strength, namely 1 in 100,000 and 1 in

50,000 dilutions of permanganate. The results are given below:

experiment, the waters were examined for coliforms to find out whether they were all killed

TABLE I

Table giving the number of instances in which KMnO_4 is reduced to different lower strengths from original higher strengths

STRENGTH OF KMnO_4 ORIGINALLY REACHED, 1 IN 200,000				STRENGTH OF KMnO_4 ORIGINALLY REACHED, 1 IN 100,000				STRENGTH OF KMnO_4 ORIGINALLY REACHED, 1 IN 50,000			
Strength to which KMnO_4 is reduced	Hours of contact			Strength to which KMnO_4 is reduced	Hours of contact			Strength to which KMnO_4 is reduced	Hours of contact		
	2	8	24		2	8	24		2	8	24
Discharged ..	8	12	17	Discharged ..	0	2	5	Discharged ..	0	0	0
1/500,000 ..	5	7	5	1/500,000 ..	1	0	1	1/500,000 ..	0	0	0
1/400,000 ..	8	6	3	1/400,000 ..	0	0	4	1/400,000 ..	0	0	0
1/300,000 ..	1	0	0	1/300,000 ..	2	4	3	1/300,000 ..	0	0	3
1/200,000 ..	3	0	0	1/200,000 ..	9	10	8	1/200,000 ..	0	0	1
				1/150,000 ..	6	8	3	1/150,000 ..	0	0	0
				1/125,000 ..	2	0	0	1/125,000 ..	1	2	7
				1/100,000 ..	4	0	0	1/100,000 ..	2	3	6
								1/ 80,000 ..	12	13	5
								1/ 70,000 ..	5	5	3
								1/ 60,000 ..	2	2	0
								1/ 50,000 ..	3	0	0
TOTAL ..	25	25	25	TOTAL ..	24	24	24	TOTAL ..	25	25	25

It will be seen that when the original strength reached was 1 in 200,000, a large number of waters, 17 out of 25, showed complete discharge of colour 24 hours after treatment; 12 out of 25, 8 hours after treatment; and 8 out of 25, 2 hours after treatment. Similar discharge of colour occurred in only 5 instances out of 24 after 24 hours, and in 2 instances out of 24 after 8 hours, when the original strength of permanganate was 1 in 100,000 there being no discharge of colour after 2 hours. There was no colour discharge even 24 hours after addition of permanganate when the original strength reached was 1 in 50,000.

(c) Relation of residual colour and the presence of coliforms

When the colour of potassium permanganate was not completely discharged in the previous

or some were still viable in spite of the colour of permanganate persisting. Table II gives the results of this observation.

It is clear from above that most of the samples which retain colour up to 2 or even 8 hours show presence of more than 2 coliforms per 100 ml. Out of the samples which retain colour up to 24 hours 4 out of 8 or 50 per cent, 5 out of 19 or 26.3 per cent, and 2 out of 25 or 8 per cent respectively of the three permanganate dilutions 1 in 200,000, 1 in 100,000 and 1 in 50,000 show presence of more than 2 coliforms per 100 ml. Thus, in the last case, 92 per cent or a large majority of samples where 1 in 50,000 permanganate is allowed to act for 24 hours show no coliforms in 100 ml.

Thus it can be concluded that retaining of colour at the end of 2 hours or even 8 hours is

TABLE II

Strength of KMnO_4	Contact period	Number of times colour not completely discharged	NUMBER OF TIMES, PRESUMPTIVE COLI PRESENT OR ABSENT IN 100 ML.		
			Absent	Present 1 or 2	Present more than 2
1 in 200,000 ..	2 hours	17	4	1	12
	8 "	13	2	2	9
	24 "	8	3	1	4
1 in 100,000 ..	2 hours	24	5	7	12
	8 "	22	4	3	15
	24 "	19	12	2	5
1 in 50,000 ..	2 hours	25	5	3	17
	8 "	25	10	3	12
	24 "	25	18	5	2

no measure of the efficacy of the permanganate in killing coliforms in water. Retaining of colour at the end of 24 hours can be more depended upon specially when the strength of permanganate is as high as 1 in 50,000.

II. Disinfecting action of potassium permanganate on coliforms

In assessing the disinfecting action of potassium permanganate on natural waters, absence of coliforms was regarded, in the present work, as a criterion for purification of water, because of the fact that coliforms are organisms which are intermediate in resistance between the spore-bearers and the comparative non-resistant intestinal pathogens. A strength of permanganate which kills the coliforms must necessarily kill intestinal pathogens. The choice of coliforms as indicator organisms thus has been thought to ensure a margin of safety in the practical disinfection in the field.

It was not however intended to exclude consideration of lethal effect of this disinfectant on the intestinal pathogens. But, it was taken up after the action of permanganate was studied on coliforms as present in water under natural conditions and taking into consideration various factors like: (a) The effect of strength of permanganate used; (b) the effect of time; (c) the effect of organic matter in amounts usually present in water; and (d) the effect of small amount of variation of pH that is usually possible.

(a) The effect of strength of permanganate used

It has been established already that retaining of the colour of permanganate up to 2 or even 8 hours in the water does not ensure the absence of coliforms and is no measure of the efficacy of permanganate used. But how far the three different strengths of permanganate used in this work, namely 1 in 200,000, 1 in 100,000, and 1 in 50,000, can kill all coliforms present in well waters is given below:

TABLE III

Strength of KMnO ₄	Period of contact	Number of times all coliforms were killed in well waters
1 in 200,000	2 hours	6 out of 29 instances (20.7%)
	8 "	5 out of 29 " (17.2%)
	24 "	6 out of 28 " (21.4%)
1 in 100,000	2 hours	5 out of 29 instances (17.2%)
	8 "	7 out of 29 " (24.1%)
	24 "	12 out of 28 " (42.9%)
1 in 50,000	2 hours	5 out of 28 instances (17.9%)
	8 "	10 out of 28 " (35.7%)
	24 "	16 out of 28 " (57.1%)

(b) The effect of time

The same table given above also shows the effect of time. The period of contact when

limited to 2 hours and 8 hours respectively gave unsatisfactory results. Taking only the 1 in 50,000 strength, 2 hours' contact made well water free from coliform in 17.9 per cent of instances, 8 hours' contact in 35.7 per cent of instances, and 24 hours' contact in 57.1 per cent of instances. The last figure is the highest so far obtained. Thus comparatively the more effective period of contact will be 24 hours.

(c) The effect of organic matter

The presence of organic matter in water markedly affects the effect of potassium permanganate. In the present work, when potassium permanganate was diluted with broth, even a strength of 1 in 25, i.e. four times the strength of phenol used in phenol coefficient tests, could not kill *Salm. typhi* under standard conditions. In nature, however, well water does not contain too much of organic matter. Organic matter content of 22 well waters, in the vicinity of Calcutta, was determined by Tidy's 4 hours' oxygen absorption test and was found to be 0.0675 part per 100,000 on the average, the figure ranging between 0.033 to 0.309 part per 100,000.

Tidy's 4 hours' oxygen absorption figure for some open wells in some villages in the districts of Bankura, Faridpore, and Burdwan in Bengal as determined by the Public Health Laboratory, Bengal, gave an average of 0.048 part per 100,000, the range being 0.011 to 0.221 part per 100,000. It appeared from the present work that when Tidy's figures for well waters were below 0.1 part per 100,000, it did not affect much the efficacy of potassium permanganate. A summary of results of the work done in this connection is given below:

TABLE IV

Tidy's 4 hours' oxygen absorption figures of well waters tested	Killing power of 1 in 50,000 potassium permanganate on coliforms in well waters acting for 24 hours
0.033 to 0.1 part per 100,000.	All coli killed in 9 instances out of 14, i.e. 64.3 per cent.
0.1 to 0.309 part per 100,000.	All coli killed in 3 instances out of 8, i.e. 37.5 per cent.

(d) The effect of pH

The average pH of 50 samples of well waters in the suburbs of Calcutta was found to be 7.36, the range of variation being from 7.0 to 8.2. The tank waters, which are more liable to pollution and generally show higher bacteriological content, were found to have a higher pH than well waters; the average of 5 samples being 8.1 and the range of variation from 7.8 to 8.4.

But before the effect of permanganate was tried, the effect of change of pH by itself was observed and is given in table V.

TABLE V

Sample number	pH	Number of coliforms per 100 ml. at the preceding pH	pH	Number of coliforms per 100 ml. at the preceding pH
1	6.8	200	7.3	900
2	6.8	13,000	7.1	2,500
3	6.8	25,000	7.0	11,000
4	6.8	168,000	7.2	35,000
5	6.8	5,000	7.0	3,000
6	6.8	3,500	7.0	3,500
7	6.8	7,000	7.0	3,500
8	6.8	200	7.0	500
9	7.0	3,500	7.2	5,000
10	7.2	1,100	7.4	800
11	6.8	5,000	7.1	7,000
12	6.8	1,300	7.0	2,000
13	7.1	4,500	7.3	8,000
14	7.1	11,000	7.3	3,500

Statistically using the 't' test the two sets of figures are not found to be significantly different. Thus, this little variation of pH by itself is of no effect on the bacterial content of water.

Next the effect of altering the pH of water along with treatment with potassium permanganate was tried. Out of 22 samples of water, whose reaction was adjusted to lower pH than its normal, 9 samples did not show any growth of coliforms after treatment with 1 in 50,000 of potassium permanganate. Hence for comparative studies, these results cannot be utilized. The results of the remaining 13 samples are given below :

TABLE VI

Sample number	pH	Number of coliforms per 100 ml. at the preceding pH	pH	Number of coliforms per 100 ml. at the preceding pH
1	6.8	25	7.2	25
2	6.8	0	7.2	1
3	6.8	0	7.2	3
4	6.6	0	7.0	3
5	6.8	8	7.2	8
6	6.8	13	7.2	50
7	6.8	25	7.2	5
8	6.8	1	7.3	0
9	6.8	90	7.0	5
10	6.8	35	7.2	35
11	6.8	5	7.0	1
12	6.8	0	7.0	35
13	7.1	0	7.3	2

Statistically using again the 't' test the two sets of figures are not found to be significantly different. Hence it may be said that the small amount of change in pH does not significantly affect the disinfectant value of potassium permanganate.

III. Disinfecting action of potassium permanganate on intestinal pathogens added to tank waters

Before a particular strength and period of contact of potassium permanganate is recommended for general use as a disinfectant of water of the usual pH and organic matter content as obtained under natural conditions, it should be ascertained how far under these conditions the pathogenic intestinal bacteria are affected.

For this purpose experiments were conducted to find out the lethal effect of potassium permanganate in the dosage used elsewhere in this work. The organisms dealt with were *Bact. typhosum* Lister, *Bact. flexner* and *Vibrio cholerae* Inaba, and the water used sterilized tank water to which these organisms were added. The results are shown in the tables that follow :

(a) Action of potassium permanganate on *Vibrio inaba* added to tank water

TABLE VII

Vibrios added to water, number per ml.	Strength of KMnO ₄	Vibrios in 100 ml. of water after contact periods of :		
		2 hours	4 hours	24 hours
1,000	1/200,000	Nil	Nil	Nil
10,000	1/200,000	"	"	"
100,000	1/200,000	"	"	"
200,000	1/200,000	Present	Present	Present
200,000	1/100,000	Nil	Nil	Nil
200,000	1/ 50,000	"	"	"
500,000	1/200,000	Present	Present	Present
500,000	1/100,000	"	"	"
500,000	1/ 50,000	Nil	Nil	Nil
1,000,000	1/200,000	Present	Present	Present
1,000,000	1/100,000	"	"	"
1,000,000	1/ 50,000	Nil	Nil	Nil

It is seen that water that may be contaminated with vibrios in a strength of 100,000 organisms per ml. or less can be effectively disinfected with 1 in 200,000 permanganate even in 2 hours.

If, however, the contaminating vibrios are 500,000 organisms per ml., neither 1 in 200,000 nor 1 in 100,000 strength of permanganate will be completely vibriocidal. A strength of 1 in 50,000 will be required for the purpose. 1 in 50,000 potassium permanganate will disinfect tank water even when it is contaminated with one million vibrios per ml. But 1 in 200,000 or even 1 in 100,000 will be useless for the purpose.

If *Shig. flexneri* contaminates water in a strength of 10,000 organisms per ml. or less, the water can be effectively disinfected with 1 in 200,000 potassium permanganate.

If the organisms are 100,000 per ml., 1 in 200,000 potassium permanganate can disinfect in 24 hours but not in 4 hours; 1 in 100,000 will

(b) Action of potassium permanganate on
Bact. flexner added to tank water

TABLE VIII

Number of <i>Shig. flexneri</i> added to water per ml.	Strength of KMnO_4	Flexners in 100 ml. of water after contact periods of :		
		2 hours	4 hours	24 hours
1,000	1/200,000	Nil	Nil	Nil
10,000	1/200,000			
100,000	1/200,000	Present	Present	"
100,000	1/100,000	"	Nil	"
100,000	1/ 50,000	Nil	"	"
200,000	1/200,000	Present	Present	Present
200,000	1/100,000	"	Nil	Nil
200,000	1/ 50,000	Nil	"	"
500,000	1/200,000	Present	Present	Present
500,000	1/100,000	"	"	"
500,000	1/ 50,000	"	"	"

disinfect in 4 hours but not in 2 hours, whereas 1 in 50,000 permanganate disinfects even in 2 hours.

If the organisms are 200,000 per ml., 1 in 200,000 of potassium permanganate is unable to disinfect even in 24 hours, though 1 in 100,000 will disinfect in 4 hours.

If, however, *Shig. flexneri* infects tank water in an amount of 500,000 per ml., even a strength of 1 in 50,000 permanganate does not disinfect.

(c) Action of potassium permanganate on
Salm. typhi added to water

TABLE IX

Number of <i>Salm. typhi</i> added to water per ml.	Strength of KMnO_4	Typhoid bacilli in 100 ml. of water after contact periods of :		
		2 hours	4 hours	24 hours
1,000	1/200,000	Nil	Nil	Nil
10,000	1/200,000			
100,000	1/200,000	Present	Present	Present
100,000	1/100,000	"	"	"
100,000	1/ 50,000	"	Nil	Nil
200,000	1/200,000	"	Present	Present
200,000	1/100,000	"	"	Nil
200,000	1/ 50,000	"	Nil	"
500,000	1/200,000	"	Present	Present
500,000	1/100,000	"	"	"
500,000	1/ 50,000	"	"	"

Typhoid bacilli, if present in tank water in a strength of 10,000 organisms per ml. or less, are easily disinfected by 1 in 200,000 potassium permanganate in 2 hours.

If these organisms are present in the higher strength of 100,000 per ml., 1 in 200,000 permanganate is useless as a disinfectant; 1 in 100,000 permanganate is unable to disinfect in 2 hours

and 4 hours, though it does so in 24 hours; 1 in 50,000 permanganate cannot disinfect in 2 hours, though it does so in 4 and 24 hours.

If the concentration of *Salm. typhi* is 200,000 organisms per ml. of water, 1 in 200,000 permanganate is unable to disinfect in 2 hours; 1 in 100,000 disinfects in 24 hours, though not in 4 hours; 1 in 50,000 disinfects in 4 hours and 24 hours but not in 2 hours.

If typhoid bacilli are present in a strength of 500,000 organisms per ml., in 50,000 permanganate cannot be depended upon to disinfect the water even in 24 hours.

In the following table the comparative effectiveness of the three dilutions of permanganate in killing the above three pathogenic organisms are given in summary form (table X).

Under practical conditions in the field well waters may not however get such a high pollution as to contain 200,000 or even 100,000 pathogenic organisms per ml. In order to know the final dilution of the pathogens in well waters contaminated by faeces of patients, an idea should be obtained of the average amount of water usually contained in wells. For this, 49 open wells near Calcutta were measured and found to contain on the average 56 c.ft. or roughly 1,500 litres of water. If 10 gm. of faeces pollute this amount of water and if the faeces contain about 1,000 million of coliforms per gm. (Suckling, 1944), the well water will contain about 5,700 coliforms per ml. If all these organisms are replaced by pathogens, they may be killed by 1 in 200,000 permanganate. But the custom in water bacteriology is to regard a water satisfactory when there are no coliforms or only 1 or 2 of them present in 100 ml. If this criterion is applied to water disinfected by permanganate, then a 1 in 50,000 dilution of it acting for 24 hours has got to be recommended, which strength in the present work is found to make waters satisfactory in 92 per cent of wells, but not in 100 per cent of them. Unfortunately, this strength will produce an objectionable deep pink colour.

Summary

1. The residual pink colour, after treatment of well waters with permanganate for 2 hours or even 8 hours, is no measure of the efficacy of the permanganate in killing coliforms, as most of the samples which retain colour up to these periods show presence of coliforms of more than 2 per 100 ml.

2. Out of the three strengths of potassium permanganate used in these experiments, 1 in 200,000 diminished coliform count in the well waters tested to 2 or less per 100 ml. in 50 per cent of instances, 1 in 100,000 in 73.5 per cent of instances and 1 in 50,000 in 92 per cent of instances. Thus, the last strength is a practically useful strength of permanganate for disinfection of water.

TABLE X

Strength of KMnO ₄	ACTION ON ORGANISMS IN WATER		
	<i>Vibrio cholerae</i>	<i>Shig. flexneri</i>	<i>Salm. typhi</i>
1 in 200,000	100,000 per ml. killed in 2 hours but not 200,000 per ml. in 24 hours.	100,000 per ml. killed in 24 hours but not 200,000 per ml. in 24 hours.	10,000 per ml. killed in 2 hours but not 100,000 per ml. in 24 hours.
1 in 100,000	200,000 per ml. killed in 2 hours but not 500,000 per ml. in 24 hours.	100,000 per ml. killed in 4 hours but not 500,000 per ml. in 24 hours.	200,000 per ml. killed in 24 hours but not 500,000 per ml. in 24 hours.
1 in 50,000	1,000,000 per ml. killed in 2 hours.	200,000 per ml. killed in 2 hours but not 500,000 per ml. in 24 hours.	200,000 per ml. killed in 4 hours but not 500,000 per ml. in 24 hours.

3. Though slight variation in pH ordinarily occurring in well waters does not significantly affect the lethal power of permanganate on coliforms, organic matter above 0.1 part per 100,000 slightly interferes with this action, when this figure is within a range of 0.033 to 0.304 part per 100,000 as in the 22 well waters examined.

4. Regarding actual disinfecting action of potassium permanganate on intestinal pathogens, when the latter were added to tank waters of the usual pH and organic matter content, of the three pathogens tested *Vibrio inaba* was found to be most susceptible. Whereas a 1 in 100,000 permanganate was sufficient to kill 200,000 vibrios per ml. in 2 hours, it took 4 hours to kill this amount of *Shig. flexneri* and 24 hours to kill the same amount of typhoid bacilli. 1 in 50,000 permanganate killed even one million of *Vibrio inaba* in only 2 hours though this strength was unable to kill 500,000 per ml. of either *Salm. typhi* or *Shig. flexneri* even in 24 hours.

Conclusions

In the disinfection of well waters with potassium permanganate, unless the reagent is used in a very strong solution of 1 in 50,000 producing an objectionable deep pink colour, it cannot be depended upon to produce a water which may be called satisfactory according to water bacteriological standards, though 1 in 200,000 dilution might kill the number of pathogenic organisms, specially cholera vibrio, that is ordinarily likely to infect well waters. With a 1 in 50,000 strength, satisfactory water could not be produced in 100 per cent of well waters, though in a large majority of them the strength will succeed after 24 hours' contact.

REFERENCE

- SUCKLING, E. V. (1944). *The Examination of Waters and Water Supplies*. J. and A. Churchill, Ltd., London.

The Indian Medical Gazette Fifty Years Ago

THE TEACHING OF HYGIENE IN INDIAN UNIVERSITIES

(From the *Indian Medical Gazette*, May 1900, Vol. 35, p. 181)

THE proposals recently made by the Committee appointed by the Faculty of Arts of Calcutta University, under the Chairmanship of Colonel T. H. Hendley, I.M.S., are such as must command the hearty approval of all who are interested in the sanitary progress of India. As medical men engaged daily in combating disease we well know that disease is scarcely as formidable a foe as ignorance. Of this the recent experience of the four years' war against plague is ample evidence. It is a common cry of a certain class of newspapers that it is not plague the people dread so much as plague measures, and Government has so far recognized this that they have endeavoured to let the people have their own way as far as possible. The question, however, may well be asked why the people should oppose measures entirely intended for their own good, and after all attended with but little inconvenience. The only reply is the ignorance of the people. All of us who have to do with the fight against plague must often have had to explain to our own subordinates who, willing enough, are yet often ignorant of the reason why such measures are decreed. That we have come to almost a deadlock in the war against plague is due to the ignorance not only of the teeming millions but to the ignorance of the better classes—the educated classes of the native community. Hygiene and sanitation is to them

merely a name, which they half understand and wholly dread. This is not as it should be. If therefore in the future India is to take her place among the civilized countries of the world, she must be educated in a better sense than she has been; we must no longer have the spectacle of the graduates of our Indian Universities opposing, with all the force of a passive resistance, measures intended for their own good, and we can see no other means of doing this than by educating the leaders and the better classes of the community. *Jo Hukum* is an admirable law where the people can do no other than obey, but in these days of Local Self-Government we must try other means. Government has recognized that what we want in India is the intelligent and willing co-operation of the people. This we can only have when the people understand that what is being done is for their own good.

No one imagines that it is possible to diffuse such knowledge among the millions of India, but surely it is possible to teach the better classes. Anyone who glances at the formidable curriculums for the various examinations in the Universities of India must acknowledge that if it is possible to teach thousands of students to understand mathematics, modern history, natural science or logics surely it is possible to teach them the elements of Hygiene. We may recall the words of Dr. Ward Cousins, the President of the last meeting of the British Medical Association, who, in his address, last year, said—'The battle against disease and death will only end in disappointment unless we have something more than the force of legislation—the great mass of the people must become active and willing helpers, the fathers and mothers of the land must learn how to maintain the healthfulness of their homes, and the blinding forces of selfishness and ignorance must be replaced by the best and purest aspirations. Depend upon it, the basis of national health is the personal cultivation of health. We desire to see a wider knowledge of the laws of health'.

The students of the Universities of India, to whom it is proposed to teach Hygiene to-day, will become the professional men, the Municipal Commissioners, etc., of to-morrow, we can well believe that if in their student days they have acquired a knowledge of the laws of health, as taught in any of the excellent textbooks proposed by the Committee, we would find them far more willing co-operators and helpers than they could possibly be without that knowledge.

For such reasons as these and because we believe that to fight successfully against disease we must first fight against ignorance we offer our cordial support to the proposals brought forward by Colonel Hendley's Committee—the first attempt as far as we know to introduce the teaching of Hygiene into any Indian University, and we express the hope that the Senate of the University will see their way to adopt the

recommendations of this Committee, a procedure which we well believe will be of great practical importance, and which we hope to see copied by the other Universities of India.

Current Topics, Etc.

Beel, J. A., Pittman, Margaret & Olson, B. J.
Pertussis and Aureomycin. Pub. Health
Rep., Wash., 1949, May 13, Vol. 64, No.
19, pp. 589-598

(Reproduced from *Bulletin of Hygiene*, Vol. 24, No. 11, November 1949, p. 838)

THIS article describes laboratory experiments on the effect of aureomycin on mice infected intracerebrally with *H. pertussis*, and also a clinical trial of the drug on 20 cases. In the experimental work, the infecting doses of *H. pertussis*, the amounts of the drug injected subcutaneously, the time intervals between infection of culture and beginning of treatment, and the frequency and duration of treatment were all varied. Groups of 10 mice were used to control each variable. In estimating results it became possible to combine the groups when the difference in protection resulting from the treatment was not significant.

It was found that treatment 72 or 96 hours after infective infection was more effective than treatment 48 hours after infection. Mice receiving large doses of the antibiotic had a substantial proportion of survivors. It was concluded that aureomycin given subcutaneously to white mice in non-toxic doses delayed and prevented deaths after intracerebral infection with *H. pertussis*. In general, a treatment regime of small doses at frequent intervals was the most effective.

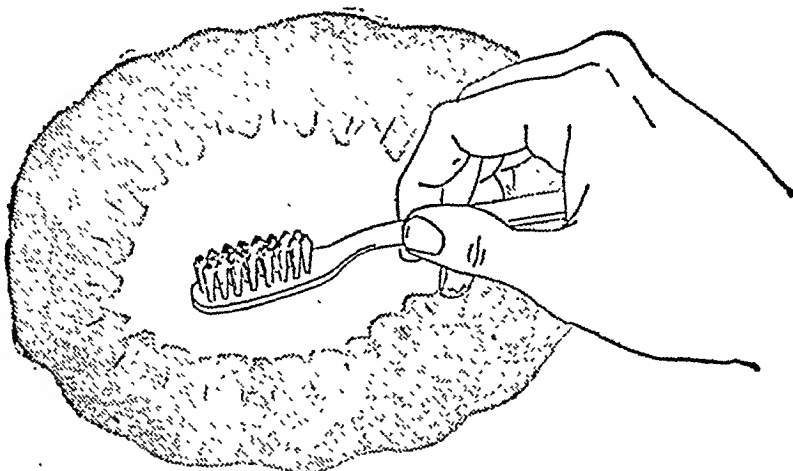
In the clinical trials the time of starting treatment varied from the second to the seventeenth day after the onset of paroxysmal cough. The dosage finally used was a total of 0.5 gm. of aureomycin per kilo of body weight given orally in divided doses over a period of eight days. The age of the patients varied from one month to six years. A comparison of the duration of paroxysmal cough in the 20 treated cases with 380 untreated cases suggests that the aureomycin shortened considerably the clinical course of the disease. In only a few cases (those that were treated early) was the response dramatic. In practically all cases a prompt but gradual diminution in the frequency and intensity of the paroxysms was observed.

Relation of Relapses in Typhoid to Duration of Chloramphenicol Therapy

By J. E. SMADEL *et al.*

(From the *Journal of the American Medical Association*, Vol. 141, 10th September, 1949, p. 129)

DURING the past year much information has accumulated on the use of chloramphenicol (chloromycetin) in the treatment of typhoid. This confirms the original report of Woodward and others, covering the observations on 10 patients, which clearly indicated that the new antibiotic was of great value in this disease. Continued experience reveals that fever disappears by lysis during the first three or four days of treatment.



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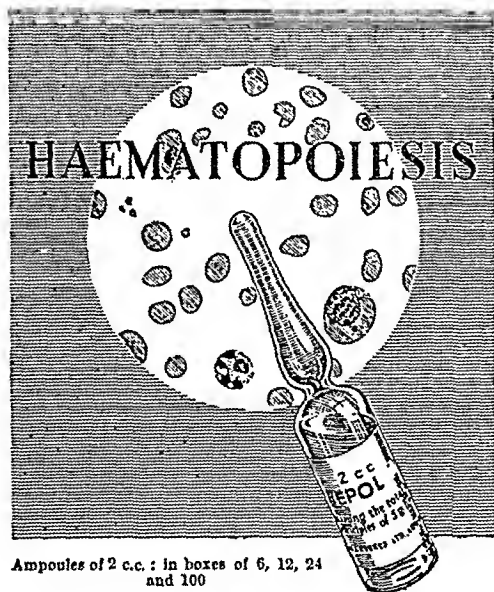
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Our early observations, as well as those of McDermott and his associates, brought out that relapses of typhoid were common in treated patients. In order to eliminate such occurrences, we have prolonged the course of treatment in persons infected with *Salmonella typhosa*. Analysis of the results obtained in 44 patients with typhoid who received chloramphenicol therapeutically under our observation has indicated a striking relation between the duration of chemotherapy and the incidence of relapses.

Although our observations are being reported in detail elsewhere, it appeared desirable to summarize certain of them at this time in a preliminary note. Following proof of the clinical diagnosis by the cultivation of *S. typhosa* from the blood, each of the 44 patients received orally an initial loading dose of 3 to 4 gm. of chloramphenicol, which was followed by 1 to 3 gm. daily given in divided doses for a variable period of time. A clinical relapse, with reappearance of bacteremia, occurred in 7 of the 13 patients whose initial course of drug was given for 8 days or less, average duration of therapy 6.9 days. None of the members of another group of 19 patients suffered relapses; this group was comparable to the first in essentially all respects, except that treatment was continued for 9 to 14 days, average 11.2. A third group consisting of 12 patients was treated for 14 to 23 days, average 18; relapses did not occur among these patients. The day of disease on which treatment was begun in the three groups averaged 13.5, 13.7 and 20.8, respectively. The total dose of chloramphenicol averaged 20.0, 25.7 and 32.8 gm. for patients in the respective groups. All patients in the first group who had relapses responded satisfactorily when chloramphenicol treatment was again instituted.

CONCLUSION

These results warrant the following conclusions. Chloramphenicol (chloromycetin) should be administered in adequate amounts for more than eight days to patients acutely ill with typhoid if relapses of the disease are to be avoided. There appears to be little advantage in continuing treatment for more than fourteen days.

Treatment of Hepatic Amoebiasis with Chloroquine

By N. J. CONAN

(From the *American Journal of Medicine*, Vol. 6, March 1949, p. 309, as abstracted in the *Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 101)

According to Conan the wartime antimalarial drug research programme disclosed a number of highly active compounds of the 4-amino-quinolone series. It seemed logical to determine whether their antiparasitodal activity extended to other pathogenic protozoa. The infection selected for study was that with *Endamoeba histolytica*, because of its relative prevalence among protozoal infections in the New York area. Of the various 4-amino-quinolone derivatives tested for antimalarial activity, the greatest amount of information was available concerning chloroquine, which is 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline, and which had proved to be one of the more active and less toxic members of the series. The author used chloroquine successfully in 7 patients with amoebic hepatitis. Chloroquine is a safe and effective chemotherapeutic agent for the treatment of amoebic infections of the liver, being at least as effective as emetine hydrochloride but without the latter's toxicity. The combination of chloroquine with a superior intestinal antiamoebic drug should permit

adequate treatment of any amoebic infection and should permit wider use of antiamoebic chemotherapy as a diagnostic and therapeutic test in obscure infections of the liver and intestine.

Aureomycin in Brucellosis

(From the *Journal of the American Medical Association*, Vol. 141, 3rd September, 1949, p. 106)

THE immediate results with aureomycin in bacteriologically proved cases of brucellosis have been more satisfactory than with other forms of available specific therapy. 'Low grade undulant fever' has come to mean ill-defined symptoms that may mimic neurasthenia, anxiety state or psychoneurosis. In these circumstances chronic brucellosis cannot be differentiated from psychosomatic dysfunction. A positive reaction to a skin test and agglutinins for brucella not only may be associated with active disease but are also found in persons who have been exposed to brucellosis in the past and have recovered. It thus becomes extremely difficult to evaluate specific therapy in an illness of doubtful causation. Therefore, even if aureomycin is tried in these cases, the results are of questionable significance. As with other infectious diseases, accurate and dependable data on specific therapy can be obtained only with bacteriologically proved cases. On this basis, aureomycin is the most satisfactory agent available for acute and chronic brucellosis due to any one of the three species of brucella.

Thioarsenites in Amoebiasis

By H. H. ANDERSON et al.

(Abstracted from the *Journal of the American Medical Association*, Vol. 140, 20th August, 1949, p. 1251)

ONE HUNDRED patients harbouring *Endamoeba histolytica* and other parasites in Memphis, Tenn., and San Jose, Costa Rica, were treated with either p-carbamidophenyl-bis (carboxymethylmercapto) arsine (C.C. 914) or p-carbamidophenyl-bis (2-carboxyphenylmercapto) arsine (C.C. 1037). These agents, in previous laboratory studies, proved approximately ten times more effective than carbarsone U.S.P. in both *in vitro* and *in vivo* tests (in naturally infected macaques).

Of 82 patients, 77 with *E. histolytica*, 3 with *Dientamoeba fragilis* and 2 with *Balantidium coli*, 74 were cleared of their parasites over a four-month follow-up period. Eighteen others, infected with *Dientamoeba fragilis* (2), *Strongyloides stercoralis* (12), *Fasciola hepatica* (1), *Leishmania tropica* (2), and *Treponema pertenue* (3), had no significant benefit following thioarsenite therapy.

Complete clinical appraisal before, during and after therapy, including tests of urine, blood and hepatic, renal and heart functions, revealed no drug toxicity due to the dose levels employed (3.0 gm. orally in ten days to 7.2 gm. in twenty-four days). In addition, 13 of these patients with acute dysentery also received C.C. 1037 in retention enemas (3.0 to 6.0 gm. in six days) with benefit and without evidence of drug toxicity to mucous membranes of the lower bowel as revealed by proctoscopic examination. No cutaneous reaction or damage to other tissues was observed. Twelve patients exhibited nausea or vomiting after 200 mg. doses of either thioarsenite. Coating of the tablets with phenyl salicylate permitted completion of therapy in all but 1 of these patients.

Three Costa Rican patients with hepatitis, who had evidence of sulphobromophthalein sodium retention

(5 to 20 per cent) at 45 minutes (before therapy), were cleared of amœbas, and their hepatic function returned to normal. One of these also required emetine hydrochloride, 0.5 gm. given parenterally over five days. Bismuth subcarbonate was also given to 2 other patients with long-standing dysentery.

Since earlier laboratory experience was confirmed, i.e. the thioarsenites are tolerated and effective in dose levels from one-tenth to one-fifth those of carbarsone, it is suggested that enteric-coated tablets of 25 to 50 mg. be employed orally, on a three times daily dose schedule over ten days. The thioarsenites in retention enemas may also be required in patients with severe dysentery.

It would appear, on the basis of laboratory and clinical trials, that the detoxication of carbarsone oxide (*p*-carbamidophenylarsenous oxide) by substituted sulphydryl groups has permitted the use of active trivalent analogues of carbarsone U.S.P. with greater distribution of an active agent to tissues, such as the liver and intestinal tract, where amœbio invasion occurs.

Myelosclerosis

(From the *Lancet*, ii, 22nd October, 1949, p. 756)

MYELOSCLEROSIS is one of those rare conditions that entrap the unwary surgeon who removes large spleens without submitting the patient to a thorough hæmatological investigation. Briefly, what happens in this disease is that the bone-marrow undergoes a curious fibrosis that slowly strangles the blood-forming elements; at the same time the spleen enlarges and blood formation begins again in its embryonic site. But this blood formation in the spleen cannot keep pace with the needs of the adult body, so the patient develops a slowly worsening anæmia; primitive white cells, even some myeloblasts, nucleated red cells, and sometimes megakaryocytes appear in the peripheral blood. The spleen becomes enormous, but if it is removed, the sole remaining site of blood formation goes, and the patient soon dies. Left alone, the patient may carry on, with diminishing efficiency and increasing discomfort, for some years. The diagnosis depends on the blood picture, the failure to obtain any cellular bone-marrow by needling, and the radiological changes in the bones. The blood picture is not characteristic, since the same picture can occur in some forms of myeloid leukaemia, and somewhat similar changes can appear in all the various diseases that cause leucocrythroblastic anæmias. Puncture of the sternum and iliac crest does not yield any cellular marrow; the final proof should be a trephine sample of sternal marrow and confirmation of the typical histological changes. Radiography sooner or later shows narrowing, or even obliteration, of the marrow cavity in the long bones, especially in the femurs.

Unfortunately the findings are not always so clear-cut and in this issue Wood and Andrews describe 3 cases that were much less typical. Differential diagnosis has given rise to much difficulty in the past, particularly between myelosclerosis and subleukæmic or aleukæmic forms of chronic myeloid leukaemia. In smears of normal bone-marrow myeloblasts, monocytes and lymphocytes are present only in small numbers; so, whatever the picture in the peripheral blood, when the bone-marrow shows large numbers of these cells, a diagnosis of leukaemia is almost certain. But in chronic myeloid leukaemia, the cells involved are myelocytes, metamyelocytes, and polymorphs, and the bone-marrow can show a majority of these cells in many other conditions besides leukaemia. The diagnosis of subleukæmic or aleukæmic chronic myeloid leukaemia thus depends on the failure to find any other cause for the enlarged spleen, the relatively few (if any) immature cells in the peripheral blood, and the demonstration

of a cellular bone-marrow perhaps containing early granulocytes—promyelocytes and myelocytes—than usual. The presence of many basophil granulocytes in the marrow is suggestive of leukaemia, and there is often a striking increase in megakaryocytes in the marrow and spleen. This condition, or one very like it, is described in America under the name 'agnogenic myeloid metaplasia' because of the granulocytic and megakaryocytic hyperplasia in sites other than the bone-marrow, again particularly in the spleen. The differential diagnosis between leukaemia and myelosclerosis may thus depend entirely on the bone-marrow findings—in leukaemia a cellular marrow with unusual numbers of granulocytes and megakaryocytes; in myelosclerosis a marrow, almost devoid of cells and largely replaced by fibrous tissue. Before bone-marrow biopsy became a standard technique, the two conditions were confused and, consequently, most of the accounts before about 1940 are not very helpful. With present knowledge the differential diagnosis can be made in most cases, and this is not merely an academic exercise, because the newer sclerosing forms of treatment, like nitrogen mustards, may be useful in leukaemia but are positively dangerous in myelosclerosis.

Poliomyelitis and Tonsillectomy

(Abstracted from the *Lancet*, ii, 3rd September, 1949, p. 424)

THE St. Pancras coroner has lately investigated the death of two young brothers, aged 7 and 4 years, who developed polioencephalitis soon after their tonsils were removed. Tonsillectomy was performed on 5th August; one child fell ill on the 18th and the other on the 19th. At the inquest a medical witness cited the warning issued by medical officers of the Ministry of Health in 1947, when the incidence of poliomyelitis was high, that there is 'overwhelming evidence that a recent tonsillectomy increases the risk of a child contracting poliomyelitis, particularly of the bulbar type where poliomyelitis is prevalent, operations on the nose and throat should, if possible, be postponed'.

Not everyone holds with this advice. At the annual meeting of the British Medical Association last year one view seemed to be that the risk, if it existed, was not such as to call for prohibition of the operation. Dr. A. M. McFarlan, however, said that recent tonsillectomy increased the danger of the disease assuming the bulbar form, and asserted that during epidemic abstinence from the operation might eliminate some of these severe cases, though it might not reduce the risk of clinical infection with the virus. And Dr. Stanley Banks claimed that the prohibition of tonsillectomy was the only useful preventive measure.

It has to be borne in mind that this year's outbreak has been characterized by an unusual number of multiple cases in families; and the coroner refused to attribute the two deaths directly to tonsillectomy. Nevertheless this tragic incident may increase the reluctance to operate when poliomyelitis is abroad: an in his letter on another page Mr. T. B. Layton comes down strongly on the side of waiting until the disease is no longer prevalent.

Myxoedematous Madness

By R. ASHER

(Abstracted from the *British Medical Journal*, ii, 10th September, 1949, p. 555)

MYXOEDEMA is one of the most important, one of the least known, and one of the most frequently misse causes of organic psychoses.

May, 1950]

Fourteen cases are here described, all of which had myxœdema and psychotic changes. In every one of them the diagnosis was confirmed beyond doubt. They all showed a psychosis amounting to complete 'madness', ten being admitted to the mental observation wards under the Lunacy Act, one referred to the neurosurgeon for cerebral tumour, and three to general medical wards with other diagnoses. In nine of the cases there was a dramatic and complete recovery of sanity with thyroid treatment, in two there was partial improvement, one showed no change, and two patients died. The fact that in none of these cases had the diagnosis been made by the outside doctor suggests that there is need for increased awareness of myxœdema as a cause of psychoses.

Cases in the literature record a very wide variety of mental changes, and certainly in the series the writer has observed there has been no constant type of psychosis, though general confusion and disorientation with persecutory delusions and hallucinations, and occasional bouts of restless violence have been common. The writer has made the diagnosis on the myxœdematous appearance of the patient and not on the kind of mental symptoms.

The following symptoms are common: general tiredness, gain in weight, vague aching pains in the legs, poor memory, constipation, deafness, falling out of hair, dry skin, always feeling cold. All these symptoms commonly occur in non-myxœdematous people and not one of them is constant in myxœdema. Change in the facial appearance, alteration in the voice, and snoring are usually noticed by relatives rather than by the patient.

The only way to ascertain what a case of myxœdema looks like is to see one. No amount of description can convey the unmistakable impression of a well-developed case. Photographs are more helpful than words, but give no idea of the characteristic colouring and voice. Here is a description of an advanced case.

Nearly all cases occur in women. The features look bloated and the normal contours of the face are smoothed away, just as the wrinkles of a balloon disappear when it is blown out. Edema collects in the lips, broadening them, and around the eyes, forming little bags of flesh beneath them. When after treatment, the swelling round the eyes subsides there is sometimes revealed a slight exophthalmos, possibly due to anterior pituitary's efforts to flog an inactive thyroid. The colour is yellowish and waxy, with a contrasting burgundy-coloured flush over the malar bones. The hair is dry and scanty, the receding hair margin leaves a wide forehead, and there may be partial baldness. The eyebrows are sparse, and sometimes the lashes too. The classical loss of hair over the outer third of the eyebrows is an unreliable sign, because so many normal people show this deficiency.

The voice is slow and fumbling from the clumsy thickness of the lips and tongue, and the œdematous infiltration of the nasal passages gives it a characteristic nasal quality. It is impossible to imprison the sound in words, but the impression is that of a bad gramophone record of a drowsy, slightly intoxicated person with a bad cold and a plum in the mouth. Snoring, already mentioned as a symptom, may be of arresting intensity, and it is odd that in a discussion on snoring at the Royal Society of Medicine, no mention was made of myxœdema as one of its causes.

The description here given is that of an unusually obvious case. The recognition of an early or a mild case is harder but is more satisfying than recognizing the self-evident one. Mild cases are probably often missed because the textbook illustrations always picture an unusually gross case and not the moderate cases which are more often encountered. Mistakes are also made through expecting every sign to be present, whereas the average case lacks at least one of the classical features of the illness.

Photographic test.—The writer considers that there is only one infallible confirmatory test for myxœdema.

Take a good photograph; then give thyroid for a month or more and take another photograph. The change between the two photographs is a clear confirmation of the diagnosis.

Blood cholesterol.—This is nearly always raised, and, furthermore, descends with thyroid treatment. Blood cholesterol estimations are, after photographs, the best confirmatory tests.

Basal metabolic rate.—From experience with many other cases besides these the writer has found the basal metabolic rate of little help in diagnosing myxœdema. It is a test which is accepted when it agrees with the physician and disregarded when it does not. I have seen many cases of myxœdema with normal or raised B.M.R. Further, the presence of mental change or respiratory obstruction may prevent the estimation being done.

Pulse rate.—The classical bradycardia of the textbook is not common. In four cases the pulse was over 70 and in only two instances was it below 60.

Blood pressure.—In six of these cases there was hypertension (either a systolic pressure above 170 mm. Hg. or a diastolic pressure above 100 mm. Hg.).

Streptomycin Treatment of Infantile Diarrhoea and Vomiting

By A. HOLZEL *et al.*

(Abstracted from the *British Medical Journal*, ii, 27th August, 1949, p. 454)

THE results of streptomycin treatment of infantile diarrhoea and vomiting are discussed.

Streptomycin was given to 26 cases orally, and to 24 intramuscularly, while a control group of 29 cases received no antibiotic.

The dosage of streptomycin was either 20 mg. per lb. body weight per day for five to seven days, or 600 mg. for the first 24 hours, followed by 450 mg. daily for a further four to six days.

The results do not indicate that streptomycin exerts any specific therapeutic effect.

The frequent association of a special type of *Bact. coli* (B.C.N.) with infantile diarrhoea and vomiting was confirmed, being found before treatment in 50 out of a total of 79 cases, but no evidence was obtained that it was of any ætiological significance.

The following two items are reproduced from Dental Newsletter No. Wa-241, March 1950, prepared by the American Dental Association:—

Theories of the Etiology of Congenital Deformities

THIS paper deals with the different aspects of congenital deformities. The problem has been attacked in a very scientific manner even though few definite conclusions were reached.

Of 100,000 pregnancies, there were 80,572 normal births, 11,765 abortions of normal embryos, 7,048 abortions of abnormal embryos and early monsters and 615 monsters born at term. Of those born at term, 1 in 132 was born with an anatomical defect.

Heredity and genetic evidence of hereditary tendencies are proved in such conditions as hemophilia, allergy, albinism and various skin dystrophies.

Hereditary characteristics are understood as being those characteristics and physical or mental traits

which are present in parents or remote ancestors and reappear among descendants in succeeding generations. This occurs by fusion of male sperm and female ova. The germ cells of the male contain particular hereditary factors called genes, which exert their action in determining future hereditary, physical or mental characteristics.

Geneticists recognize three groups of inherited defects: (1) recessive—the group in which the abnormality may occur in one or more sibs, but less often in their children or parents; (2) dominant—the group in which the deformity is transmitted by direct descent from affected members of a family to some of their children, who in turn transmit it; (3) sex-linked—the group in which the abnormality is transmitted by normal females and affects only males of the family.

A person with a dominant anomaly mating with either a normal or a heterozygous person stands a 1 to 1 chance of producing an anomalous offspring; a 3 to 1 chance with a recessive. In case of sex-linked inheritance the relationship is 1 to 1 and 1 to 1, the daughter carrying the anomaly and the sons being affected.

Genes undergoing mutation will alter and confuse the picture of the expected result in mating.

Frequently congenital deformities tend to predominate in the male with an associated left-sided predominance, particularly striking in harelip. Warkany cites Fortuyn's conclusions that harelip and cleft palate are inherited as a double recessive trait, one gene being autosomal and the other sex-linked, hence the predominance in the male.

A statistical study revealed that males and females were affected equally by congenital deformities. From 607 cases it was found that malformed children were born more often to older mothers.

Of 275 families investigated it was found that 12.4 per cent of the families produced one or more congenitally malformed members. This is important because parents with a malformed child have a chance to repeat the deformity in another child.

(W. S. Kiskadden, M.D., A. M. Schechtman, Ph.D., and Clayton Brock, M.D., Surgery, Gynecology and Obstetrics: *International Abstract Surgery*, 88, 1, January 1949.)

Procaine Penicillin with Aluminum Monostearate

A GROUP of 150 patients requiring antibiotic therapy were studied to collect material for this article. Both deposit forms of penicillin and oral tablets were used. In the group of 110 patients given penicillin intramuscularly, procaine penicillin G suspended in peanut oil with 2 per cent aluminum monostearate was the preparation used. In an attempt to evaluate the effectiveness of this preparation as a therapeutic agent, varying dosage schedules and dosages were employed. The resulting serum levels of penicillin determined by carefully checked laboratory procedures were thoroughly tabulated. Assuming that 0.03 unit per cubic centimetre of serum was a minimum desirable therapeutic level, the author found that the serum level was adequate in 90 per cent of patients 72 hours after a single injection of 300,000 units, while adequate levels were reached in the first hour after injection. Multiple dosage schedules gave sustained high serum levels depending on the dosage used and the frequency of administration. No foreign body reactions to the injected material were noted clinically. The author also was able to correlate higher levels immediately after injection and lower levels after 24 hours with active and ambulatory patients.

Observations were made on serum levels resulting from the administration of eight different preparations of oral tablets. One hundred thousand unit buffered

tablets with 2 grammes of aluminum monostearate were compared with 500,000 and 1,000,000 unit tablets, some buffered and some unbuffered. The conclusions reached were that no oral tablet produced an adequate level after eight hours, though buffered tablets did maintain a slightly higher level after eight hours.

To supplement this timely study, the drug reactions encountered in the series are reported and described. In those patients receiving the drug intramuscularly, only 1 had a reaction. In the series of 40 patients given oral penicillin 2 were seen. The 3 patients were treated with antihistaminic drugs.

(Jean M. Robinson: *Journal of Michigan State Medical Society*, 48, 337, March 1949.)

The following four items are reproduced from Medical Newsletter No. Wa-216, January 1950, prepared by the American Medical Association:—

Continuous Intravenous Injection of Typhoid Vaccine in Treatment of Certain Ophthalmic Diseases

CURRY AND SHAW point out that for many years artificial fever, induced in a hypertherm cabinet or by injections of foreign protein or typhoid vaccine, has been used in the treatment of various diseases of the eye. Attention has been directed particularly toward the use of single, rapid intravenous injections of typhoid vaccine. A drawback of this type of therapy is the unpredictable febrile reaction. Moreover, typhoid therapy is frequently withheld from elderly patients or persons with heart disease because of the risk entailed in a severe reaction. Solomon and Somkin in 1942 introduced the method of controlled hyperpyrexia by the continuous intravenous administration of typhoid vaccine. It occurred to the authors that this type of therapy might well be applied to the treatment of certain ophthalmic diseases.

One cubic centimetre of typhoid vaccine in a concentration of 1,000,000,000 killed organisms per cubic centimetre was suspended in 1 litre of sterile isotonic sodium chloride solution U.S.P. With the patient in bed, a 21 gauge intravenous needle was inserted in an antecubital vein and the mixture allowed to flow at a rate of 20 to 30 drops per minute. Rectal temperatures were recorded at fifteen-minute intervals. If the temperature did not begin to rise in 30 to 45 minutes, the rate of flow was doubled. If the rise in temperature was rapid, the rate of flow was decreased. The degree of fever desired varied from case to case, depending on the condition under treatment and the physical condition of the patient.

Summarizing their experience with this method the authors say that a total of 17 patients with ophthalmic diseases, including non-specific iritis, syphilitic keratitis and suspected sympathetic ophthalmia, were treated by the continuous intravenous administration of typhoid vaccine, with gratifying results in every case. This method of treatment is recommended because it may be given safely to elderly and debilitated patients and the degree of fever and chilling may be controlled.

(Curry, J. J., and Shaw, E. A.: *Archives of Ophthalmology*, 42, 123-125, August 1949. The authors are connected with the Robert Dawson Evans Memorial and the Ophthalmologic Service, Massachusetts Memorial Hospitals, Boston, Mass.)

Flocculation Tests in the Diagnosis of Hepato-Biliary Disease

STEIGMANN and his associates performed the cephalin cholesterol flocculation, thymol turbidity, thymol flocculation, Gros, Takata-Ara and zinc sulfate

turbidity tests on 324 persons, which included normal persons, patients with miscellaneous diseases without conspicuous involvement of the hepato-biliary tract and patients with diseases of this tract. It was found that all flocculation tests have a significant number of abnormal results in miscellaneous diseases and some of them (e.g. thymol turbidity) even in normal persons.

Most of the flocculation tests, especially thymol turbidity, cephalin flocculation, zinc sulfate turbidity and Gros tests are as a rule normal or only slightly abnormal in liver cell damage produced by non-infected extrahepatic biliary obstruction (biliary hepatitis). With the exception of the zinc sulfate turbidity test they become abnormal if biliary hepatitis is complicated by bacterial infection of the portal triads.

The flocculation tests are of greatest value in the differential diagnosis between surgical and medical jaundice, especially the zinc sulfate turbidity and cephalin flocculation tests; more so even, if considered together and if secondary bacterial infection of the portal triads is accounted for by the clinical septic manifestation. The flocculation tests are of less value for the separation of acute hepatitis from cirrhosis. In this the Takata-Ara test is most helpful; however, a combination of zinc sulfate and thymol turbidity and Gros tests reduces the number of errors.

The tests are of least value in the separation of conditions with and without liver cell damage except that a higher number of abnormal results in the different tests points to liver cell damage.

Of the tests studied the cephalin flocculation appears most specific if abnormal and the zinc sulfate turbidity if normal in the presence of jaundice. The additional performance of the thymol turbidity and Gros tests is helpful in the solution of most problems met in the differential diagnosis of hepato-biliary disease. Consideration of the results of several tests has advantage over that of individual tests.

(Steigmann, Chicago, Ill., Popper, H., Hernandez, R., and Shulman, B.: *Gastroenterology*, **13**, 9-19, July 1949. The authors are connected with the Hektoen Institute for Medical Research, and the Departments of Pathology, and Internal Medicine and Therapeutics of the Cook County Hospital, and the Department of Pathology, North-Western University Medical School, and the Department of Internal Medicine, University of Illinois College of Medicine, Chicago, Illinois.)

Chorea (Sydenham): A Study of Fifty-eight Additional Patients

KAGAN and his associates say that in a previous investigation on 107 patients with Sydenham's chorea it was observed that chorea with an increased erythrocyte sedimentation rate was in most instances associated with active rheumatic fever. Patients who (in the absence of cardiac failure) had a normal erythrocyte sedimentation rate during the early part of their chorea had no symptoms or signs of rheumatic disease at that time or at any time during a long follow-up period.

In this report, the results of a study of 58 additional patients with chorea are presented. The aim was to determine whether data collected from various sources under relatively less uniform conditions would yield results similar to those obtained in the previous study in which the data were collected at one individual hospital (Michael Reese Hospital). At the various hospitals electrocardiograms, erythrocyte sedimentation rates and roentgenologic examinations were performed in different ways and interpreted along slightly different lines.

In spite of the different sources and methods, the data obtained proved to be essentially similar to those

reported from the Michael Reese Hospital. These observations lend further support to the concept that Sydenham's chorea is not always associated with rheumatic fever and that, specifically, an initial episode of such chorea in a person with a normal erythrocyte sedimentation rate and no other evidence of rheumatic fever is probably not due to rheumatic fever.

The authors recommend that these latter cases be referred to as 'Sydenham's chorea of undetermined cause' in order to avoid the implication that they are due to rheumatic fever with all its possible sequelae.

Association with rheumatic fever is quite likely in cases in which the first episode of chorea is accompanied by an increase in the erythrocyte sedimentation rate. In the absence of other rheumatic manifestations, however, it is difficult to establish with certainty that these patients have rheumatic fever. In other words, a diagnosis of 'chorea (Sydenham), associated with rheumatic fever', should be made only when there is other evidence of rheumatic fever.

Patients who have chorea associated with rheumatic fever may have similar recurrences or may have recurrences during which there are no other evidences of rheumatic fever. Patients who have chorea which is not associated with rheumatic fever ['chorea (Sydenham), cause undetermined'] may be expected to have recurrences which are also not associated with rheumatic fever, and as a group they may be expected to experience no greater incidence of rheumatic fever or its sequelae than does the general child population.

(Kagan, B. M., Chicago, Ill., Rosner, D., and Rosenblum, P.: *American Journal of Diseases of Children*, **78**, 306-313, September 1949. The authors are connected with the Medical Research Institute of Michael Reese Hospital, Chicago, Illinois, and other Chicago hospitals.)

Mumps Meningoencephalitis with and without Parotitis

KILHAM points out that clinical and epidemiologic observations concerning mumps meningoencephalitis have been confirmed by adequate diagnostic evidence from the laboratory only quite recently and in few accounts. Kane and Euders were the first to use serologic methods in a comprehensive study of the disease, and Henle and McDougall demonstrated the ease of virus isolation.

In the present study of 25 patients with mumps meningoencephalitis, 13 with no enlargement of the salivary glands, conclusions were based on cases diagnosed by means of a combination of the newer techniques of serologic study and virus isolation. Cerebrospinal fluid in amounts of 0.2 cc. was inoculated into the amniotic sacs of 7-day-old embryonated eggs, which were then incubated at 35°C. (95°F.) until the thirteenth day. The amniotic fluids were tested separately for the presence of virus by agglutination of hen erythrocytes. The result was confirmed by subsequent passage through eggs, using pooled amniotic membranes and fluids when hemagglutination was absent and only the fluid when hemagglutination occurred. No spinal fluid was judged free of virus until three egg passages were negative. Samples of saliva were centrifuged, treated with penicillin and streptomycin and examined in similar fashion. Strains of virus isolated by these methods were identified as mumps virus by the antihemagglutination test, using paired serums from patients known to have experienced a rise in mumps antibodies.

The clinical reaction that characterized these 25 patients with mumps meningoencephalitis was similar to that reported in recent summaries. Meningeal irritation was variously marked by headache, nausea, vomiting and nuchal rigidity. A few children had

convulsions and delirium. One significant feature was the impossibility of distinguishing by clinical means between the signs and symptoms of patients with mumps meningoencephalitis and those of others who had serologically negative reactions for mumps and such clinical diagnosis as non-paralytic poliomyelitis and lymphocytic meningitis.

Seven of 12 patients who had both meningoencephalitis and parotitis showed the two conditions on the same day. In five others parotid swelling preceded encephalitis five to nine days and had subsided by the time the patient came to the hospital.

All but five of the 25 patients were males. The average duration of the illness was eight days. A few developed sequels. Pleocytosis, with a high percentage of lymphocytes, characterized the spinal fluid of patients with mumps meningoencephalitis.

A total of 12 patients served as controls for the group with serologically proved mumps meningoencephalitis: six patients with uncomplicated mumps parotitis and six with disease of the central nervous system determined not to be mumps by serologic test. Mumps virus was isolated from the spinal fluid of more than half of the patients with confirmed mumps infection of the central nervous system and in no instance from that of the control series.

All of the 25 cases of mumps meningoencephalitis reported have occurred between March and November 1948, a year in which mumps was unusually prevalent in Massachusetts. Cases of meningoencephalitis associated with parotitis were scattered more or less regularly throughout the period, but 11 of the 13 patients with meningoencephalitis and no parotitis were seen from mid-May to early September. As the numbers are small, they may represent no more than chance distribution. The hypothesis is suggested, however, that enlargement of the salivary glands is a less frequent manifestation of mumps in summer than in winter.

The author feels that mumps meningoencephalitis, with or without parotitis, is in certain years a common form of lymphocytic meningoencephalitis among children and young adults. Knowledge of the true incidence of the disease, especially when no glandular swelling is apparent, will await further application of newer diagnostic methods to a study of epidemics of mumps occurring within closed groups. No other encephalitis can be identified more readily by serologic methods, for the antihemagglutination test is simple and as satisfactory as complement fixation in establishing a diagnosis of mumps. A serologic test is indicated whenever appropriate signs and symptoms are associated with a spinal fluid having 150 to 2,500 leukocytes per cubic millimetre, of which 95 per cent are lymphocytes, and an elevated total protein content and, especially, with a history of exposure to mumps.

(Kilham, L., Boston, Mass.: *American Journal of Diseases of Children*, 78, 324-333, September 1949. The author is connected with the Department of Epidemiology, Harvard School of Public Health, Boston, Mass.)

Science and You

By MAURICE GOLDSMITH

UNESCO Science Editor

(Reproduced from UNESCO Features, No. 17, 15th March, 1950, p. 10)

NEW QUALITIES FOUND IN MOTHERS' MILK

IMMUNIZATION of pregnant and nursing mothers may finally put an end to the deaths of newborn babies from such killers as diphtheria and whooping cough. During the dangerous first few months of life, according to recent scientific research, infants can thus gain additional powers of resistance until they can, them-

selves, undergo vaccination. This new advance in the fight against disease is foreshadowed in now being carried out at the world-famous Pasteur Institute in Paris.

Behind this work lies the recognition that infectious diseases—a serious threat to the unborn and newly born child—must be fought through the mother.

It has been known for some time that during pregnancy there are anti-toxic substances which circulate in the blood-stream of the mother and pass into the fetus through the placenta. These give the child a natural resistance to certain infections.

However, immunization acquired in this way is not lasting. These research workers have discovered a method of securing this. It is possible to do so by ensuring that from birth the child is fed exclusively on the mothers' milk.

Until this work, done by M. M. Lemétayer and Nicol, it was believed that the anti-toxins which give immunity to the child were transmitted only through the placenta. New disease-protection: discovered, however, by an analysis of colostrum—a liquid secreted by the mammary glands of women shortly before the birth of a child and during the first few hours after the birth.

The presence of a large quantity of anti-toxins was found in the colostrum of mothers who had been immunized against diphtheria. These anti-toxins, it was believed, could give an important reinforcement to the immunity already transmitted by the placenta.

Strong anti-diphtheria and anti-tetanus immunity, through the appropriate vaccinations, were given to several women before they gave birth. Samples of the colostrum liquid were taken from each woman during the first eight and twelve hours after birth, and before the first feed. Analyses showed three things: first, that the colostrum contained variable quantities of anti-toxins; second, that each newborn child had at birth a quantity of anti-toxins proportional to the immunity received by the mother; and third, that the immunity of the child was only slightly reduced after birth when it was breast fed.

The conclusion that may be drawn is that it would be advisable to immunize all mothers just before confinement, so that the immunity transmitted to the child through the placenta is maintained by the milk. The stronger the vaccination, the longer will the immunity last. Proof of this was given when a foal, whose mother had been re-vaccinated four months after birth, kept this immunity for several months more, whereas normally the immunity ended towards the fiftieth day after birth.

These doctors at the Pasteur Institute feel that the vaccination of a pregnant woman is a guarantee that the infant will be rendered immune from certain childhood illnesses, especially in the case of tetanus for which there is no natural immunity.

Again, the diphtheria anti-toxin, which is derived from a natural source, has been discovered in the colostrum, but was not present in the milk on the tenth day. Thus, it is advisable to give artificial immunization, which is more lasting.

It is possible to transmit, through the mother, a reinforcement to natural resistance to infection by children. It is interesting to note that Dr. Philip Cohen of New York—states Marguerite Clark, in her book "Medicine on the March"—has urged that all mothers be inoculated against diphtheria and whooping cough during the last three months of pregnancy. This is the time when anti-bodies and anti-toxins pass most easily from the mother to the child. The immunity will not only protect the pregnant woman against these diseases, but will immunize her baby for the first few months of his life until he is ready for his own inoculation schedule. The shots may cause a mild local reaction in the mother but they will not harm the pregnancy.

These experiments—of which I have given but the barest outline—are of fundamental importance. First, they give authoritative reinforcement for a call to inoculate pregnant and nursing mothers. Second, they may put an end to the old controversy about the merits of artificial as against breast-feeding. This is a problem of importance mainly in the more industrialized areas of the world where artificial feeding has largely replaced mothers' milk as the principal source of substance for infants.

It is known that newborn children who are artificially fed are, on the whole, less resistant to illnesses such as tetanus, diphtheria and whooping cough.

In any event, the scientific case for the oft-repeated claim that 'the mothers' milk cannot be replaced' has been further reinforced (UNESCO).

'Positive Cure' Claimed for Tubercular Meningitis

(Reproduced from UNESCO Features, No. 17, 15th March, 1950, p. 9)

THE elimination of tubercular meningitis as a cause of death may be achieved through proper use of streptomycin, according to a report submitted to experts from 14 nations who met recently in Paris. It was stated that this formerly incurable disease can be given 'positive cure'. An Italian scientist reported 82 per cent success in his Florence clinic, by means of injected doses of the anti-biotic drug.

The Paris conference brought together streptomycin experts from 13 European countries and the United States. The experts stressed the urgency of continued international shipments of the drug and essential diagnostic equipment.

In terms of treatment, the scientists recommended uninterrupted injections of streptomycin long past the supposed time of 'cure' of tubercular meningitis. They also suggested uniform methods of reporting results in the uses of the drug, for international statistical pools. Tubercular meningitis is one of the infections of the membranes of the spinal cord and brain, occurring usually in childhood.

The meeting of experts was jointly sponsored by the United Nations International Children's Emergency Fund, the World Health Organization and the International Children's Centre of Paris (UNESCO).

Reviews

THE BRITISH PHARMACEUTICAL CODEX, 1949.—Published by Director of the Council of the Pharmaceutical Society of Great Britain. The Pharmaceutical Press, 17, Bloomsbury Square, London, W.C.1. Pp. 1562. Price, £3 3s. 0d.

The British Pharmaceutical Codex was first issued in 1907 for the use of medical practitioners and pharmacists, and it contained information on all drugs and medicines then in common use. It soon came to be recognized as a standard book of reference, successive issues appearing at intervals until interrupted by the war. At the end of 1945, the work of revision was intensified, and the present volume is the product of long painstaking labour on the part of the Codex Revision Committee and the sub-committee of the Pharmaceutical Society.

There is much in this volume that is of interest and of practical value to medical practitioners. It gives facts about drugs and their preparation together with

concise statements of their action and uses. It embraces all official drugs and preparations, and also those not included in the British Pharmacopoeia, so that it meets practically all the requirements of the practitioners. The book is arranged into the following six parts: (1) general monograph on chemical substances and drugs of vegetable and animal origin, beginning with acaia and ending with zingiber, and including some such substances as tea, coffee and yeast; (2) antisera and vaccines; (3) preparations of human blood, including human fibrinogen and human thrombin; (4) surgical ligatures and sutures; (5) formulary, representing creams, dusting powders, elixirs, capsules, tinctures, injections, etc.; and (6) appliances, giving miscellaneous information. The book should be a valuable addition to any doctor's library.

R. N. C.

PRACTICE OF ALLERGY.—By Warren T. Vaughan, M.D., revised by J. Harvey Black, M.D. Second Edition. 1948. The C. V. Mosby Company, St. Louis. Pp. xx plus 1132, with 333 illustrations in black and white

THE second edition of this comprehensive work has appeared after 9 years and after a revision by another worker who has retained the 'quality and flavour' of the original while adding new material and removing old which is no longer necessary or acceptable.

Ten pages of contents, 20 of index and 37 of bibliography, all in small print, indicate what has been given in this book of 1152 pages, consisting of 16 parts and 79 chapters. Nothing appears to have been missed.

Parts specially full of information are V, VI and VII dealing with Food Allergy and Inhalant Allergy. All that grows lives, or moves in the U.S.A., and can produce allergy has been documented and illustrated. The moulds have another section devoted to them in addition. Details of making extracts of the offending substances and of techniques of tests and treatment are available. So are the reasons for apparent obscurities. An allergic could eat lobsters caught north of Cape Cod but not those caught south of that point. The difference lay in the food supply of the lobsters: the supply from the Gulf stream and southern waters was different from that derived from the Arctic current. Unlike what holds in Europe R is the name of the month for eating oysters is not necessary in the United States because no disease occurs in oysters in the summer months, nor is the spawning confined to the summer months there.

Physical allergy though covering only 6 pages is very informative. 'How does cold act? I believe in three ways. First: As a local irritant. Second: As a stimulant to the cutaneous surfaces. In no other way can be explained the immediate production of asthma by cold to the feet. Third: By producing catarrhal bronchitis. In the first two cases the cold acts at once.

'How do heat and thunder act: I believe by producing greater general irritability of the nervous system and making it more sensitive to sources of disturbance of any kind whatever.'

(This is a quotation in the book from other authors. Many such quotations occur throughout the book on other subdivisions of allergy also.)

The part dealing with pharmacology of allergy gives all up-to-date therapeutic measures, including endocrine preparations and vitamins.

Towards the end of the book are given the diseases caused or kept going by allergy.

One need not be frightened by 'a surprisingly large number of sudden deaths after tetanus antitoxin injection' mentioned by the author on the authority of unpublished work personally communicated to him by an army surgeon of the World War II (pp. 844-845). The reviewer has looked after soldiers of both the World Wars and has had no cause for anxiety.

Sidelights are available on many items such as the history of silk culture in Europe (under silk allergy). In 552 A.D. two monks smuggled silkworm eggs from China and started the industry at Constantinople under the protection of Emperor Justinian.

The get-up is of a high order.

An excellent publication for all interested in allergy.

S. D. S. G.

PSYCHOSOMATIC MEDICINE: THE CLINICAL APPLICATION OF PSYCHOPATHOLOGY TO GENERAL MEDICAL PROBLEMS.—By Edward Weiss, M.D., and O. S. English, M.D. Second Edition. 1949. W. B. Saunders Company, Philadelphia and London. Pp. xxx plus 803. Price, 47s. 6d.

PSYCHOSOMATIC medicine is a mode of approach to illness in which both the soma and the psyche are studied; it therefore consists in supplementing, but not supplanting, physical techniques of medical investigations with psychological ones. This applies specially to a very large proportion of chronic patients with or without definite bodily disease, the root cause of whose troubles is emotional disturbance. The subject is however not quite new, for in the past there have been some who could see beyond the disease to the patient in the background. Even in the ancient days the Greeks regarded the body and mind as one and undivided, and Plato had said, 'this is the great error of our day that physicians separate the soul from the body'. Only latterly owing to the development of laboratory methods and instruments of precision the medical practice has become too mechanistic in character with the result that the individual behind the disease has been somewhat forgotten. Many physicians are well aware that emotions and feelings of their patients have some connection with the diseases from which they suffer, but their understanding of the underlying causes is rather vague and obscure. To-day, thanks to the genius and work of Freud, Jung and Adler, great light has been shed in the field of human behaviour and it is now possible by psychological methods to ascertain a patient's attitude and reaction to life.

In this book Prof. Weiss and Prof. English deal with the relationship of emotional factors and physical disease, their diagnosis and how to handle them. It is divided into two parts: (1) general aspects of psychosomatic medicine, including diagnosis and treatment, and (2) special applications to general medicine and the specialities. The book is remarkable for its lucidity, and it can be easily understood by practitioners not trained in psychological theories. Here they will find . . . cardiac neurosis, hypertension, peptic ulcer, climacteric disorders, asthma, etc., described in a very instructive manner. Its value is enhanced by numerous records of cases such as are seen in general practice. In this edition the authors have included the experience of military medicine in the last war and many other studies on psychosomatic disorders. Of late there has been a spate of books on psychosomatic medicine; this book is perhaps the best we have yet seen.

R. N. C.

MEDICAL ETYMOLOGY.—By O. H. Perry Pepper, M.D. 1949. W. B. Saunders Company, Philadelphia and London. Pp. 263. Price, 27s. 6d.

THIS book is the natural outcome of the change that has come over the pre-medical education of the medical students in America and England. They do not now know Latin and Greek as a rule. This lack of knowledge the book supplies.

The book is not a medical dictionary; but its less than 4,000 terms give almost all the roots the student will encounter in some 50,000 terms usually found in a medical dictionary

Further, the book advocates dispensing with worry about strictly proper endings. Once a word has entered English terminology and assumed English citizenship it must live, move and end like other citizens.

The terms are arranged alphabetically in 4 parts: introduction, preclinical subjects, clinical subjects and dentistry.

The book will be specially useful in India where Latin and Greek were hardly ever learnt by medical students.

S. D. S. G.

GENERAL CYTOLOGY.—By E. D. P. De Robertis, M.D., W. W. Nowinski, Ph.D., and F. A. Saez, Ph.D. Translated by W. Andrew, Ph.D. 1948. W. B. Saunders Company, Philadelphia and London. Pp. xi plus 345. Illustrated. Price, 27s. 6d.

THIS book is intended for students of medicine, agronomy, veterinary medicine and natural sciences. It introduces into cytology several items not included ordinarily, such as physical chemistry, microspectrophotometry, plant hormones, in fact, novelties which may bewilder rather than encourage the beginner.

Sub-micro . . . cells, plasma membrane and . . . items.

The detailed description of chromosomes, cell division and cytogenetics take up nearly a quarter of the book with diagrams which are not unlikely to strike most of the students for whom the book is meant, as figments of the geneticist.

Visible manifestation of cellular activity is again a useful item.

The end deals appropriately with theories of cell senescence, death and post-mortem modification.

The book falls short of expectations on the minute structure of (i) spermatozoa and ova, the custodians of life, and (ii) the cells of the central nervous system, those elders among cells, which serve a whole life time without renewal or regeneration, unlike other cells.

S. D. S. G.

FEMALE SEX ENDOCRINOLOGY.—By Charles H. Birnberg, M.D. Published by J. B. Lippincott Company. Pp. 134 with 30 illustrations including 3 colour. Price, 24s. net

IN this little book of 134 pages the author has presented all uncontroversial knowledge on the subject in a comprehensive way. For all endocrine diseases and disorders in females, including lack of ovulation, schemes of treatment by hormones are given in full. Details of office (small laboratory for clinical purpose in a physician's surgery) procedure including the examination of the semen of a partner, in sterility, are also given.

Illustrations are excellent. Differential staining in plate 2 needs an explanation.

The get-up is very good. The price could be lower.

An excellent publication.

S. D. S. G.

HYGIENE.—By J. R. Currie, M.A. (Oxon.), M.D., LL.D. (Glas.), D.P.H. (Birm.), F.R.C.P. (Edn.), and A. G. Mearns, M.D., B.Sc. (Public Health), D.P.H. (Glas.), F.R.S. (Edn.). Third Edition. 1948. E. and S. Livingstone Ltd., Edinburgh. Pp. xx plus 724 with 212 illustrations and 4 plates in colour. Price, 35s.; postage, 9d. (home)

THE third edition of this book has been completely revised; it has undergone some increase in size in consequence of new material and new figures, tables and plates. It is a good textbook on hygiene, especially designed for students in which the current teaching has been presented in a lucid and attractive style. It deserves to be widely used.

R. N. C.

A TEXTBOOK OF PHYSIOLOGY.—Originally by William H. Howell, M.D. Edited by John F. Fulton, M.D., Sterling Prof. of Physiology, Yale University Medical School. New Sixteenth Edition. 1949. W. B. Saunders Company, Philadelphia and London. Pp. xi plus 1258 with illustration on 558 figures. Price, 50s.

THIS well-known book of physiology, originally by William H. Howell, has now reached the sixteenth edition. There are new chapters on the endocrines, electrocardiograms, gastro-intestinal tract, muscle cerebrospinal fluid and the physiology of micturition. All the other chapters have been exclusively revised and brought up to date. By deleting obsolete material and making a judicious selection of new material, Dr. John Fuller and his collaborators have produced a balanced work without at the same time lengthening the text.

R. N. C.

THE CLINICAL EXAMINATION OF THE NERVOUS SYSTEM.—By G. H. Monrad-Krohn, M.D., F.R.C.P. Ninth Edition. 1948. H. K. Lewis and Co., Ltd., London. Pp. xx plus 459 with 131 illustrations. Price, 16s. net

THIS book has appeared in its ninth edition after one year only. It is a book 'from the clinic for the clinic' and not intended as a textbook of clinical neurology. In it will be found new symptoms (cushion sensation in toes, page 41; compass gait, page 155), old symptoms seen from a new angle (opisthotonos in quadrigeminal syndrome) and new tests (Sulkowitch test, page 8), new graphs of development of nervous disturbances and disabilities (decursus morbi, pages 1 to 3).

Angiography provides further details. It appears to have been considered more favourably by the profession recently.

Considered opinions of a renowned neurologist are also available: (1) There is no doubt that many neurotic complaints are accentuated by constipation; (2) repetition of examination constitutes an unintentional re-education.

The author has drawn attention to a remarkable difference between the patients in a neurological clinic to-day and 27 years ago: To-day they are early cases, 27 years ago they were advanced cases. New signs and symptoms have been recognized with the passage of time, and they help in detecting and treating early cases.

The reader used to seeing familiar illustrations in English and American books will see a new lot in the book.

In this edition photographs are included in the text, not pasted separately as before.

A very readable little book.

S. D. S. G.

AIDS TO FORENSIC MEDICINE AND TOXICOLOGY.—By W. G. Altchison Robertson, M.D., D.Sc., F.R.C.P.E. Edited by J. H. Ryffel, B.Ch., B.Sc., F.R.I.C. Twelfth Edition. 1949. Baillière, Tindall and Cox, 7 and 8, Henrietta Street, London, W.C.2. Pp. x plus 170. Price, 4s. 6d.

THE twelfth edition of this little book remains a proof of the fact that it takes a big scholar to write a small book.

Subtleties of this important subject need several modes of presentation. The 'Aids' is one of the modes. It presents all essentials in a nutshell. Even original observations are available: (1) Whitney's formic acid test of blood. It is an improvement on hæmin crystals. (2) A difference between legitimate and lawfully begotten. (3) Characteristic seminal odour on moistening the seminal stain. (4) In responsibility, the 'right or wrong' test *versus* 'power of controlling his actions'. (5) Emetics will not act in phenol poisoning. The reader will find many more useful

points. Only the statement on poisonous fungi is more definite than it should be.

The get-up remains of a high order.

An excellent publication.

S. D. S. G.

BOOKS RECEIVED

1. Report on the Maritime Trade of Bengal for the Official Year, 1946-47. By O. Krishnan, M.A. Published by the Manager of Publications, Delhi. Printed by the Government of India Press, Calcutta, India. Rs. 5 or 8s.

2. Malaria Control in the British Colonies. Issued by British Information Services, Eastern House, Man Singh Road, New Delhi.

3. The Miscellany. Vol. XVI, No. 8, February 1950. Managing Editor: Dr. P. A. S. Raghavan, Z.M.R.E. (Vienna), Teppakulam, Timelirapalli.

4. Genetic-Statistical and Psychiatric Investigations of a West Swedish Population. By Torsten Sjogren, Ejnar Munksgaard Norregade 6—Copenhagen, 1948. Price: 15 Dan. Crowns.

5. Microphthalmos and Anophthalmos with or without Coincident Oligophrenia: A Clinical and Genetic-Statistical Study. By Torsten Sjogren and Tage Larsson. Ejnar Munksgaard Norregade 6—Copenhagen, 1949. Price: 15 Swed. Crowns.

6. Nutrition Research Laboratories: Indian Research Fund Association, Coonoor, South India. A History of Its Origin, Development and Activities. By V. N. Patwardhan, Director.

7. Indian Journal of Neurology and Psychiatry (Published Quarterly). Organ of the Indian Psychiatric Society. Vol. 1, No. 3, 1949. Editor: Dr. Nagendranath De. Editorial and Business Office, 128-B, Dharamtalla Street, Calcutta 13, India. Annual subscription: Inland Rs. 8; abroad 15s. or \$3.

8. The Eleventh Maharashtra and Karnatak Provincial Medical Conference, Dharwar, Welcome Speech. By Dr. S. M. Kuradikeri, L.C.P.S., President. 1950. Printed and published by Mr. V. R. Koppel, M.A., B.T., Superintendent, Tontadarya Press, Dharwar.

9. The Eleventh Maharashtra and Karnatak Provincial Medical Conference, Dharwar. Presidential Address by Dr. M. S. Wagale, L.M.&S., Gadag, 1950. Printed by M. G. Palekar at the Vasant Printing Works, Dharwar. Published by Dr. K. S. Kamalapur, Secretary, Eleventh Maharashtra and Karnatak Medical Conference, Dharwar.

10. The Eleventh Maharashtra and Karnatak Provincial Medical Conference, Dharwar, 1950. By Sjt. R. A. Jahagirdar, M.A., LL.B., Vice-Chancellor, Karnatak University, Dharwar. Printed at Mohan Press, Dharwar.

Abstracts from Reports

ANNUAL REPORT ON THE WORKING OF THE ASSAM MENTAL HOSPITAL, TEZPUR, FOR THE YEAR 1948. BY COLONEL A. N. CHOPRA, O.B.E., M.B., B.S. (PB.), D.T.M. (LIV.), D.P.H. (ENG.), I.M.S. 1950. PRINTED AT THE ASSAM GOVERNMENT PRESS, SHILLONG. PRICE, RS. 2-9-0 OR 3s. 10d.

THE total number of patients treated during the year under report was 860 (727 males and 133 females) as against 840 (706 males and 134 females) in the

previous year. Of this number, 45 males and 6 females were discharged 'cured', 47 males and 8 females were discharged 'improved', 5 males and 1 female were transferred, 1 male was discharged as 'otherwise', 26 (20 males and 6 females) died, leaving 721 (609 males and 112 females) at the end of the year. All the 51 persons discharged 'cured' were non-criminal mental patients.

The types of insanity among admissions and re-admissions were as follows :—

Manic depressive psychosis	16
Melancholia	1
Mania	3
Schizophrenia including—			
Dementia præcox	125
Epilepsy and epileptic insanity	4
Acute confusional insanity	1
			150

Mortality.—There were 27 deaths, including one observation case during the year against 40 in 1947. The chief causes of deaths were dysentery and tuberculosis which together (12 and 5) accounted for 17 out of a total of 27 deaths.

Excluding receipts from paying patients and miscellaneous receipts which were credited to the Government, the total expenditure for the upkeep of the Mental Hospital amounted to Rs. 3,71,445-8-3 against Rs. 2,93,028-14-0 in the previous year. The average cost per head was Rs. 510-3-4 against Rs. 409-10-0 in 1947.

Employment of patients.—Mental patients are employed in cultivation of vegetables, sugar-cane, jute, manufacture of gur, fencing of garden, bamboo works, carpentry, tailoring and in daily routine of clearing hospital premises and disinfecting of clothing and cooking of food, etc.

Female patients are employed in paddy husking, preparation of spices, mending of clothes and other household work.

Weaving is done by female patients. The female section of the hospital is, to some extent, self-supporting in the matter of cotton clothing.

With the appointment of an Occupational Therapist, patients are being employed in weaving with one fly-shuttle loom purchased during the year. Experience has shown that, given the opportunity, more patients can be employed in this useful work which, in addition to providing the much needed occupational therapy, will help enable the patients to use clothings manufactured by themselves. Arrangements are being made to have another fly-shuttle loom.

Treatment : Mental.—Occupational therapy continues to occupy the important position. Maniacal outbursts and insomnia are treated with hypnotics and hydro-therapy.

The hospital lacks in equipment of modern type for better treatment facilities. Sanction for the purchase of a shock therapy apparatus has since been accorded by Government.

There is no provision for nursing sisters for the female section and male nurses for the male inmates. But in an institution like this nurses are of imperative necessity.

At present only the Superintendent and Deputy Superintendent have some training in mental diseases. Another Assistant Surgeon Grade II attached to the hospital was sent to the Inter-Provincial Mental Hospital, Ranchi, for training in Psychiatry in January 1949. For better management and more efficient working increase in the strength of the superior and inferior staff is necessary.

R. N. C.

THE 83RD ANNUAL REPORT OF THE CHEMICAL EXAMINER TO GOVERNMENT UNITED PROVINCES, AGRA, FOR THE YEAR ENDING 31ST DECEMBER, 1947.

Medico-legal section.—One thousand two hundred and ninety medico-legal cases and 4,824 articles were examined during the year under report as against 1,326 cases and 4,494 articles in 1946.

Human poisoning.—The total number of cases examined under this head was 331. Poison was detected in 61.6 per cent of cases as against 62.4 per cent in 1946.

Datura was the most commonly used poison. It was detected in 32.4 per cent of the detected cases.

Opium, arsenic, alcohol, aconite, bhang and strychnine came in order of frequency forming 25.0, 17.1, 4.9, 4.4, 3.9 and 2.5 per cent respectively of the detected poisons. Other inorganic poisons were detected in 6.4 per cent of the detected cases and other organic poisons in 3.4 per cent of the detected cases.

In 182 cases, including 4 cases of abortion, viscera were received. Poison was detected in 59.9 per cent of these cases as compared with 57.4 per cent for the year 1946. This low percentage of detection is mainly due to the fact that a large number of cases was received in which the cause of death was other than poisoning. In thirty cases death was due to causes like drowning, serious multiple injuries, hanging, strangulation, colic, pneumonia, forcible miscarriage, shock and prolonged illness.

In 68 fatal cases, no post-mortem report was received and in many cases no history or information of any kind was given by the forwarding officer.

Remains of cremation (alleged poisoning). Bones and ashes of six persons were received and examined during the year. Traces of arsenic were detected in all of these cases.

The largest number of cases of fatal poisoning was received from Agra, viz. 16, followed by Lucknow 9, Mainpuri 6, Jaunpur 6, Meerut 6 and Kanpur 6.

Animal poisoning.—Twenty-two cases were examined under this head as compared with 22 cases for the preceding year. The percentage of detection in these cases was 72.7 as compared with 36.4 for the year 1946.

Arsenic was detected in 6 cases, strychnine in 3 cases, Aconite in 2 cases, Kaner (yellow oleander) in 2 cases, opium, mercury and madar (*Calotropis gigantea*) in one case.

Stain cases.—Nine hundred and thirty-three cases were examined under this section comprising 723 cases of blood stains. Two hundred and ten cases of blood and semen stains (sodomy and rape cases).

Three thousand seven hundred and fifty-six articles alleged to be stained with blood, semen, etc., were received in connection with 933 cases for examination against 3,282 articles received in connection with 905 cases in 1946. The percentage of detection in blood stain cases (murder or hurt by violence) was 95.5 as compared with 95.0 per cent for the year 1946. Spermatozoa were detected in 95.7 per cent of cases of sexual offence as against 99.5 for 1946.

General section (including excise).—Two thousand three hundred and forty-nine articles were examined as compared to 2,387 examined during the year 1946.

Contraband opium.—Three hundred and twenty-four samples of opium were received in connection with illicit traffic. Of these samples 238 were found to be contraband or adulterated.

The largest number of cases of illicit distillation was referred from Unao 66, followed by Meerut 49, Fatehpur 45, Bulandshahr 34, Basti 32, Faizabad 27, and Shahjahanpur 23.

Medico-legal cases of interest have been referred to in the report.

R. N. C.

ADMINISTRATION REPORT FOR THE YEAR 1948-49. K. E. M. HOSPITAL AND G. S. M. COLLEGE

Dr. R. G. DHAYAGUDE, continued to hold the post of the Dean during the year. He was deputed by the Corporation to attend the International Conference on Tropical Diseases and Malaria at Washington.

During the year under report, the Advisory Medical Board held nine meetings inclusive of one general meeting of the honorary and professorial staff. The deliberations of the education committee of the Advisory Medical Board, revived since October 1945, proved useful for discussion of important educational questions affecting these institutions.

The 510 beds of the hospital were fully occupied during the year under report. The total number of patients admitted during the year 1948 was 20,843 against 18,152 and 17,096 during 1947 and 1946 respectively.

Out of the total number of 21,383 in-patients (20,843 admitted during the year under report and 540 previous year's balance), 8,636 were cured, 7,004 were discharged relieved, 3,046 either left the hospital against medical advice or were otherwise discharged and 2,079 died (excluding three still-born infants), leaving a balance of 618 patients at the end of the year. Out of 2,079 deaths, 609 died within the first 24 hours of admission, 564 died after 24 hours but within 3 days of admission and the remaining 906 died more than three days after admission into the hospital.

The highest number of out-patients attendance on any one day during the year 1948 was 3,090, the highest number of new admissions in the outdoor department on a single day being 818. Likewise, the highest number on a single day of old cases treated was 2,370, of casualty cases 142 and of in-patients admitted 96.

The total expenditure incurred on the maintenance of the hospital during the year, including liabilities outstanding at the end of the year and exclusive of cost of the extension scheme amounted approximately to Rs. 17,91,503 inclusive of dearness allowance of about Rs. 3,09,098. This expenditure includes the cost of maintenance and treatment of in-patients, the cost of the out-patient department, the resident, medical, nursing and labour staff as well as that of the staff for administration and the maintenance and repairs of buildings, etc.

The actual cost incurred on patients (in-patients as well as out-patients) under drugs, surgical appliances, etc., is, however, exclusive of the cost of the expensive drugs, injections, blood transfusions, etc., met out of the Poor Box Charity Fund amounting to Rs. 87,834-6-0 during the year as was done in previous year.

The arrangement of sending two nurses every month to the Arthur Road Hospital to attend on fever cases was continued during the year. During the year, 25 nurses for junior examination and 19 nurses for senior examination were trained, out of whom 24 and 16 have passed respectively in junior and senior examinations held by the Bombay Nurses, Midwives and Health Visitors Council. The cost of the nursing establishment worked out at Rs. 145-9-8 per nurse, per mensem, against Rs. 145-4-11 in the preceding year. The Nurses' Welfare Fund inaugurated for promoting the welfare of the nursing staff of this hospital continued to be of material help to them.

The treatment of school children attending the Municipal Primary Schools was continued during the year under report. The total number of children treated in the year was 6,333 as against 5,310 in the previous year.

The Poor Box Charity Fund from which relief is rendered to poor patients by providing them with spectacles, crutches, artificial limbs, travelling expenses, etc., has received steady support from the public as well as from the patients of this hospital. Besides

relief in the shape of blood transfusion, costly drugs, medicines, injections, travelling expenses, etc., the special appliances were provided to 138 patients at a cost of Rs. 2,777-12-0.

Donations to the extent of Rs. 18,589-6-9 were received and acknowledged with thanks during the year.

The Co-operative Credit Society of the labour staff of the hospital and college worked satisfactorily. The total number of members on the roll at the end of March 1949, was 568 against 532 on the corresponding date of the previous year. Sixty-eight new members joined the Society and 32 left it during the period owing to death or termination of service.

The share capital of the Society increased from Rs. 64,922-3-0 to Rs. 85,917-12-0. The amount of loans granted was Rs. 1,02,960 and the amount refunded was Rs. 86,946. The average amount of loan granted was Rs. 235-9-0.

The Society held its last annual general meeting on 29th October, 1948, and declared a dividend of 5 per cent for the year ended on 30th June, 1948. The net profit during the year ended on 30th June, 1948, amounted to Rs. 4,713-1-6. The reserve fund of the Society stood at Rs. 4,961-6-3 and the total of other funds at Rs. 1,983-12-6 on the 31st March, 1949.

During the year under report, 82 fresh admissions were made. An educational survey of these students shows that their average age at the time of their admission was 19 years, it being 16.6 years when they matriculated. The corresponding ages in the previous year were 18.9 years and 16.6 years respectively. Eighty-one of these students were single and one betrothed. A statistical study of the occupations of the parents or guardians of the newly admitted students showed that 29 were dependent on service, 26 on business, 10 on medical profession, 3 on legal profession, 3 on pensions, 6 on landed property and 5 on miscellaneous occupations.

The number of undergraduate students on the college roll at the close of the year was 536, which included 132 lady students, and that of post-graduate and research students was 91.

The total expenditure of the college including the expenditure on the hostels came to Rs. 3,41,878 during the year as against Rs. 3,27,180 during the year 1947-48. In addition to the above expenditure the amount spent on payment of dearness allowance came to Rs. 85,795. The revenue of the college in the form of tuition fees, hostel rent and miscellaneous receipts amounted to Rs. 1,96,661 as against Rs. 1,57,786 during the year 1947-48. The gross cost per student for the year under report was Rs. 797.9 while the net cost worked out at Rs. 431.0 as compared with the corresponding figures of Rs. 675.2 and Rs. 394.5, respectively, for the year 1947-48. The amount of fees received from the post-graduate students was Rs. 15,004.

During the year 1948-49, 272 books were added to the Library as against 203 books in the preceding year.

New wet and dry specimens were added to the Anatomy Museum during the year and 20 old specimens were renewed. Twenty-five old specimens which had gone bad were removed from the Museum. No substantial addition could be made to the number of specimens in the Anatomy Museum owing to inadequate supply of dead bodies and jars of the required size for mounting specimens. The total number of wet and dry specimens in the Anatomy and Comparative Anatomy Sections now comes to about 1,711. Students from different schools from the City and Bombay Suburban Districts and nurses from different hospitals in the City were allowed to visit the Anatomy Museum during the year.

In the Pathology Museum 148 new specimens were mounted during the year bringing the total number of specimens to 1,603.

In the Artist's Department 845 photographs of patients, specimens, etc., were taken during the year.

The number of students residing in the hostel for male students during the year under report was 147. In addition 20 more students were provided accommodations as a temporary measure by allowing two students to stay in some of the larger corner rooms.

The number of lady students residing in the lady students' hostel during the year under report was the same as in the previous year, viz, 28. Accommodation on a temporary basis was provided to 18 more lady students in the vacant rooms in the Nurses' Home. Both the hostels were thus fully occupied and several applications for rooms had to be rejected for want of vacancies. A pressing need for the extension of both the hostels is keenly felt.

The total expenditure incurred on the hostels was Rs. 19,825, while the income derived in the form of rent was Rs. 23,201.

The annual athletic sports for this year were held on the college play-ground.

The Gymkhana took part as usual in the inter-collegiate tournaments during the year.

Thirty students were selected to join the National Cadet Corps.

The different departments of the college and the hospital had, in addition to their normal teaching and departmental work, research investigations in hand during the year. Some of the enquiries were carried out under the auspices of the Indian Research Fund Association.

The report ends with 20 appendices.

R. N. C.

BRIEF REPORT ON HOSPITALS AND DISPENSARIES FOR THE YEARS 1941 TO 1945 TOGETHER WITH ANNUAL REPORT FOR THE YEAR ENDING 31ST DECEMBER, 1946. GOVERNMENT OF THE CENTRAL PROVINCES AND BERAR. GOVERNMENT PRINTING, C. P. AND BERAR, NAGPUR. 1949

Hospitals and dispensaries.—At the close of the year 1940 there were 392 hospitals and dispensaries while at the close of the year 1945 there were 399 hospitals and dispensaries in the province. The increase of the dispensaries was in the rural areas.

Medical personnel.—The strength of the medical personnel gradually decreased, obviously due to demand on them for duty in the armed forces. There was, however, a gradual increase in the strength of the midwives and a small increase in the strength of the salaried graduates.

Indoor patients.—The number of beds available in the State—Public, Local Fund and Private—Aided Hospitals in the province for the in-patients gradually rose from 1,509 in 1941 to 1,613 in 1945 and from 1,093 in 1941 to 1,285 in 1945 for men and women, respectively.

The total number of indoor patients treated increased steadily, except for a small decrease in 1942, from 52,198 in 1941 to 59,257 in 1945.

The daily average number of the patients showed a relative increase from 1,885 in 1941 to 2,076 in 1945.

There were 2,660 deaths among the total indoor patients treated in the year 1941 and 3,592 in 1945, the ratio, thereof, to the total treated being 5.10 to 5.39 per cent.

Outdoor patients.—The total number of outdoor patients showed a decline from the year 1941 to the year 1945. This was due to the fact that at many of the rural dispensaries medical officers were not available, being deputed for the military duty. Their work was carried out either by one medical officer looking after two nearby dispensaries, periodically, or by a compounder.

Sick treated in all classes of medical institutions.—In addition to the number of beds in the State—Public, Local Fund and Private—Aided Hospitals in the province, there was an increase in the number of

beds for both men and women from the year 1941 to the year 1945.

Malaria remained the chief prevailing disease during the period under review, Akola, Buldana, Raipur, N. were other chief districts where malarial incidence was predominant.

Other principal diseases for which relief was sought were scabies, diseases of eye, ear, nervous system, respiratory system (excluding tuberculosis and pneumonia), diarrhoea, dysentery (amoebic and bacillary), other diseases of the digestive system (excluding diarrhoea, dysentery and tumours), pyrexia of uncertain origin, influenza, rheumatic fever, venereal diseases and pneumonia.

The number of outdoor and indoor patients treated for tuberculosis of lung increased from 4,811 in 1941 to 5,558 in 1945. This was mainly due to the increasing popularity of the tuberculosis clinics in the province opened in 1937.

Surgical operations.—The total number of surgical operations performed during the period under review was 565,013.

Financial condition.—The opening cash and closing cash balances in 1941 were Rs. 7,89,229 and Rs. 5,03,213, respectively, and the respective figures for the year 1945 were Rs. 6,73,856 and Rs. 5,87,409.

The total receipts of all the hospitals and dispensaries taken together showed a general improvement as seen from the total receipts of Rs. 23,37,699 in 1941 to Rs. 29,13,524 in 1945. Relatively, there was an increase in the total expenditure, viz, Rs. 15,90,554 in 1941 to Rs. 23,26,115 in 1945.

Invested capital.—The balance of the invested capital of State—Public, Local Fund and Private—Aided and subsidized dispensaries was Rs. 10,85,292 on 31st December 1941 and it rose to Rs. 14,13,305 in 1945.

R. N. C.

ANNUAL REPORT ON CIVIL HOSPITALS AND DISPENSARIES IN THE CENTRAL PROVINCES AND BERAR FOR THE YEAR ENDING 31ST DECEMBER, 1946

Eight new dispensaries were opened and three dispensaries were closed during the year under review.

There were four subsidized medical practitioners in the province during the year. There were 26 subsidized Ayurvedic and Unani dispensaries and 58 Ayurvedic dispensaries in the province during the year. Government have sanctioned 11 scholarships for the training of Vaidyas and Hakims.

During the year seven posts of sub-charge assistant medical officers have been sanctioned.

Five Anti-Malaria Units have been sanctioned under the Director of Public Health, Central Provinces and Berar. Two of these units are in full commission—one in Nagpur and the other at Nawapara (Raipur)—where carefully conducted experiments in malaria control under village conditions are being carried out. A sum of Rs. 35,000 has been allocated for municipal anti-malaria schemes. Grants have been made to the municipalities at Gondia, Saugor, Mandla and Nawapara. Five trucks have been sanctioned by Government for the Anti-Malaria Units.

An allocation of Rs. 1,54,000 has been made by Government as this year's contribution to the scheme for the establishment of homes for burnt out cases of leprosy as annexes to existing institutions at Champa and Chandkhuri. A grant-in-aid of Rs. 3,000 has been sanctioned for extension to the Maharogi Sewa Mandal at Wardha.

In pursuance of the Medical Department Post-War Development Schemes for the general increase of medical staff for hospitals, clinics and dispensaries, Government have sanctioned the deputation of six doctors and six health visitors for training in tuberculosis work outside the province during the financial year 1946-47.

R. N. C.

Correspondence

PENICILLIN AND SULPHADIAZINE IN LOBAR PNEUMONIA

SIR,—In lobar pneumonia cases I have been using penicillin injections simultaneously with sulphadiazine and have always had good results. The clinical response in almost all cases has been quick and complications and mortality have been almost nil. I can say many hopeless cases survived when chances of such survival were very remote. My own experience is that the two drugs used simultaneously give better results than either drug used separately.

Recently I read in *Diseases of the Chest*, Chicago 15 : 255-376, March 1949, that Volini *et al.* compared the results of the treatment of lobar pneumonia with sulphadiazine, penicillin and the two together. They found that in the group in which sulphadiazine was given with penicillin there was delayed clinical response, a greater incidence of complications and a higher mortality. Their observation proved that there was an antagonistic effect on each other instead of synergistic one.

Please let me know your views about the value or otherwise of the combined use of the two drugs in lobar pneumonia.

Yours faithfully,

MAJOR S. CHATTERJEE, M.B., D.T.M.

[Will readers kindly give their experience.—EDITOR, I.M.G.]

HEPARIN IN YELLOW FEVER

SIR,—Over 40 years ago Calmette (1908) noted that lesions resulting from the injection of viper venom 'Strangely resembled those observed in the case of individuals who have died from yellow fever'. Calmette further states that this observation was made by several scientists, notably Snamelli, and that it had probably lead Dyer and Bettineour to treat—without much success—yellow fever by the antitoxin of venom.

It is not surprising that antivenene should be of little or no value in the treatment of yellow fever despite similarity in the pathology of the two conditions, for such sera are of course purely specific in action. Nevertheless, if the action of yellow fever virus resembles that of viper venom, it may be that a non-specific physiological antidote to venom will be of some value as an antidote to the action of the virus.

In heparin we have a physiological antidote to the venom of the Russell's viper (*daboia*), as shown by Ahuja *et al.* (1946). On purely theoretical grounds, unsubstantiated by any experimental work on our part, we suggest the use of this anticoagulant in the treatment of experimental yellow fever in monkeys.

We apologize for so speculative a theory, but as we are precluded from experimentation on yellow fever in India, we write in the hope that some one in a position to conduct such work may give the suggestion a trial.

Yours faithfully,

CENTRAL RESEARCH INSTITUTE,
KASALI,

9th May, 1950.

M. L. AHUJA

and

A. G. BROOKS.

REFERENCES

- AHUJA, M. L., BROOKS, A Note on the Action of A. G., VEERARAGHAVAN, Heparin on Russell's Viper N., and MENON, Venom. *Ind. Jour. Med. Res.*, Vol. XXXIV, No. 2, I. G. K. (1946). pp. 317-322.
- CALMETTE, A. (1908) .. 'Venoms, Venenous Animals and Antivenomous Serum,' John Bale, Sons and Daniellson Ltd., London.

AN APPEAL

To

The Members of the Indian Medical Association and Indian Medical Profession.

ON account of the recent migration of Hindus from East Bengal to West Bengal and of the Mohammedans from West Bengal to East Bengal, there has been a large number of people collected at the Frontiers. Owing to the inadequacy of the sanitary arrangements, they suffer from one disease or the other and great and urgent need of medical relief was felt. The Bengal Provincial Branch of the Indian Medical Association has appointed Bengal Relief Committee to organize and co-ordinate medical relief operations for the unfortunate displaced brothers and sisters and several centres for medical relief have been opened in that area. Large funds were necessary for the medical relief work. The Indian Medical Association donated an amount of Rs. 10,000 from its Benevolent Fund for rendering relief to the unfortunate doctors displaced from Eastern Pakistan and a sum of Rs. 3,015 from its Distress Relief Fund for other medical relief activities. The Bengal Medical Relief Committee finds it necessary to continue the medical relief even after the Delhi Pact. The amount donated by the Indian Medical Association is almost utilized. They need more funds to continue their activities.

I have, therefore, to request each and every member of the Indian Medical Association and of the Medical Profession to contribute their might towards the Bengal Medical Relief and to send their donation direct to the Bengal Provincial Branch, Indian Medical Association, 67, Dharamtala Street, Calcutta 13. The receipt will be sent direct to the donor and it will be also acknowledged in the *Journal of the Indian Medical Association*. I hope the medical profession in India will rise to the occasion and do their best to the Bengal people in their times of distress.

Yours faithfully,

CHAMANLAL M. MEHTA,

President,

Indian Medical Association.

SHRI NIWAS,
SANDHURST ROAD,
BOMBAY 4,
25th May, 1950.

I.M.G. PREVIOUS ISSUES

SIR,—I need the following volumes of *Indian Medical Gazette* to complete my collections :—

1. Vol. LXXXVIII, Nos. 1 to 8, 1943.
2. Vol. LXXXIX, Nos. 2, 8, 9 and 10, 1944.
3. Vol. LXXX, No. 1, 1945.

Messrs. Thacker, Spink and Co. (1933), Ltd. are unable to supply these volumes. I however feel that some medical institutions or medical men may have spare copies of these volumes and would be only too glad to spare if a request is made to them.

I would therefore request you to put in a note to this effect in your next issue of the *Indian Medical Gazette*.

Yours faithfully,

A. S. GAREWAL,

LIEUTENANT-COLONEL, I.M.S.,

NAGPUR,
27th May, 1950.

Director of Health Services,
Health Section, Madhya Pradesh.

Service Notes

APPOINTMENTS AND TRANSFERS

Dr. K. C. K. E. RAJA is confirmed in the post of Director-General of Health Services, with effect from the 1st June, 1948.

Lieutenant-Colonel C. K. Lakshmanan, Director, All-India Institute of Hygiene and Public Health,

Calcutta, was placed on deputation abroad from the 3rd February to the 14th March, 1950.

On return from deputation, Lieutenant-Colonel B. L. Taneja assumed charge of the post of Medical Superintendent, Irwin and Safdarjang Annexe Hospitals, New Delhi, with effect from the 15th March, 1950 (forenoon).

The services of Major N. Jungalwalla, an officer of the late Indian Medical Service (Civil), are placed at the disposal of the World Health Organization for appointment as Regional Adviser in Venereal Diseases, with effect from the 4th January, 1950.

Dr. P. V. Benjamin, Adviser in Tuberculosis, Directorate-General of Health Services, was placed on deputation abroad from the 5th June to the 10th August, 1949.

Dr. R. L. Mehra on relinquishment of charge of his office of officiating Medical Superintendent, Irwin and Safdarjang Annexe Hospitals, New Delhi, and on expiry of the leave granted to him, has been re-posted as Senior Medical Officer, Port Blair, with effect from the date he takes over charge of his duties at Port Blair.

On return from leave, Dr. C. B. D'Silva, officiating Assistant Director, Central Research Institute, Kasauli, resumed charge of his duties at the Institute on the 2nd February, 1950.

Dr. M. N. Lahiri is appointed Associate Professor of Microbiology at the All-India Institute of Hygiene and Public Health, Calcutta, for a period of five years, with the first year on probation, with effect from the 15th February, 1950.

On return from deputation, Dr. A. B. Roy Chowdhury resumed charge of the post of Second Assistant to the Serologist and Chemical Examiner to the Government of India, Calcutta, with effect from the afternoon of the 25th February, 1950.

On relief by Dr. A. B. Roy Chowdhury, Dr. D. N. Majumdar resumed charge of the post of Fourth Assistant to the Serologist and Chemical Examiner to the Government of India, Calcutta, with effect from the same date.

Drs. Naranjan Singh and Gurkirpal Singh, ex-I.M.S. (I.C.), are confirmed as Medical Assistants at the Central Research Institute, Kasauli, with effect from the 21st March, 1950.

Mr. C. B. Naidu, Factory Manager, Medical Store Depot, Madras, was appointed to officiate as Deputy Assistant Director-General (Medical Stores), Medical Store Depot, Madras, from the afternoon of the 24th October, 1949, to the 8th February, 1950 (afternoon).

Miss T. K. Adranvala, Chief Nursing Superintendent in the Directorate-General of Health Services, was placed on deputation from the 17th February to the 1st March, 1950, to Geneva to attend the meeting of the Expert Committee on Nursing of the World Health Organization. She resumed charge of the post of Chief Nursing Superintendent in that Directorate on the 2nd March, 1950.

LEAVE

Major L. S. F. Woodhead, an officer of the late Indian Medical Service (Civil), was granted leave preparatory to retirement for 11 months and 1 day (*viz.* leave on average pay for 5 months and 29 days followed by leave on half-average pay for the remaining period), with effect from the 4th July, 1947.

Captain K. A. De'Rozario, Depot Manager, Medical Store Depot, Bombay, was granted leave on average pay for 1 month from the 9th August to the 8th September, 1949. He was allowed to prefix Sunday, the 7th and the holiday on 8th August, 1949, to his leave.

Dr. S. N. Chakraverty, a temporary Assistant Depot Manager, Medical Store Depot, Karnal, was granted terminal leave on average pay for 34 days with effect from the 24th January, 1950.

Lieutenant-Colonel M. K. Kelaykar, Drugs Controller, India, is granted leave on average pay for 1 month, with effect from the 6th March, 1950.

Dr. R. L. Mehra, officiating Medical Superintendent, Irwin and Safdarjang Annexe Hospitals, New Delhi, was granted earned leave for 28 days, with effect from the 15th March, 1950 (forenoon).

Dr. R. L. Mehra, officiating Medical Superintendent, Irwin and Safdarjang Annexe Hospitals, New Delhi, has been granted earned leave for a further period of 11 days in extension of the leave already granted, with permission to suffix Sunday, the 23rd April, 1950. His services are placed at the disposal of the Ministry of Home Affairs on the expiry of the leave.

RELINQUISHMENTS

The undermentioned gentlemen ceased to hold the honorary appointments shown against their names on the Personal Staff of His Excellency the Governor-General, with effect from the afternoon of the 25th January, 1950 :—

Major-General A. N. Sharma, Honorary Surgeon.

Major-General D. R. Thapar, Honorary Surgeon.

Colonel B. P. Baliga, Honorary Surgeon.

Colonel S. L. Bhatia, M.C., Honorary Surgeon.

Colonel R. K. Tandon, Honorary Surgeon.

Dr. R. V. Rajam, Honorary Civil Surgeon.

Dr. Gokul Narayan Vyas, Honorary Civil Surgeon.

Dr. Amalanada Das, Honorary Civil Surgeon.

Dr. E. V. Srinivasan, Honorary Ophthalmic Surgeon.

Dr. M. N. Lahiri, an officer of the Medical Research Department (on probation) and officiating Assistant Director, Central Research Institute, Kasauli, relinquished charge of his duties on the 6th February, 1950 (afternoon).

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CONTENTS

	Page		Page
ORIGINAL ARTICLES		REGISTER OF SCIENTIFIC PERSONNEL :	
Outbreak of Kala-azar in an Institution in Bombay. By Y. M. Bhende, M.D., N. M. Purandare, M.D., D. D. Banker, M.D., N. Figueredo, M.B., B.S., B.Hy., and S. D. Desai, M.B., B.S. ..	237	'ENGINEERS' VOLUME PUBLISHED ..	265
Tumours of Endothelial Origin. By B. P. Tribedi and A. K. Dutta Gupta ..	239	MENACE OF THE 'DUSTED' LUNG : WORLD EXPERTS MEET AT SYDNEY. By C. C. D. Brammall ..	265
Pneumococcal Meningitis with Atypical Features. By N. R. Konar, M.D. (Cal.), M.R.C.P. (Lond.) ..	245	MALARIA CONTROL IN CEYLON ..	267
Rheumatoid Arthritis in a Child with Unusual Manifestations. By S. K. Mukherjee, M.B. (Cal.), M.R.C.P. (Lond.), D.T.M. & H. (Lond.) ..	247	CZECHOSLOVAKIA WITHDRAWS FROM W.H.O. DESPITE ONGOING PROGRAMME IN THE COUNTRY ..	267
The Incidence and Distribution of Murine Typhus amongst Bombay Rats. By D. W. Soman ..	249	6,000,000 DOLLAR INTERNATIONAL PROGRAMMES FOR HEALTH IMPROVEMENT IN ASIAN COUNTRIES ..	267
Streptomycin in Syphilis. By B. B. Gokhale, M.B., B.S., D.V. & D. (Bom.), and S. N. Ranade, B.Sc., M.B., F.C.P.S. (Bom.) ..	253	W.H.O. ANTIBIOTICS PROGRAMME DRAFTED BY EXPERTS : RECOMMENDATIONS TO THIRD WORLD HEALTH ASSEMBLY ..	268
A MIRROR OF HOSPITAL PRACTICE		THIRD WORLD HEALTH ASSEMBLY TO OPEN ON 8TH MAY ..	268
A Case of Sciatica due to Malaria. By Amrit Lal Wahi, M.B., B.S. ..	255	THIRD WORLD HEALTH ASSEMBLY OPENS IN GENEVA : W.H.O. DIRECTOR-GENERAL'S APPEAL FOR NATIONAL INVESTMENT IN HEALTH ..	269
A Case of Intestinal Infestation with <i>Hymenolepis diminuta</i> in Man. By A. S. Parande, L.M.P., D.T.M. ..	256	WORK OF LEPER MISSION IN INDIA ..	270
An Unusual Case of Lymphocele of the Scrotum. By B. P. Tribedi ..	256	DRUGS RULES, 1945 ..	270
A Case of Acute Tingling. By Madan Mohon Ghose, M.B. (Cal.) ..	257	DRUGS ACT, 1940 ..	270
THERAPEUTIC NOTES		TWENTY-THREE INDIAN DOCTORS TO ATTEND CONGRESS OF RADIOLOGY ..	270
Notes on Some Remedies. XXXIV. Dehydration and its treatment : Treatment of cholera. By R. N. Chaudhuri, M.B., M.R.C.P., T.D.D. ..	257	FIFTY YEARS AGO	
EDITORIAL		TUBERCULOSIS IN INDIA (<i>Indian Medical Gazette</i> , June 1900, Vol. 35, p. 222) ..	271
Against Pessimism in Tuberculosis ..	261	CURRENT TOPICS, ETC.	
MEDICAL NEWS		CHLORAMPHENICOL IN TREATMENT OF INFANTILE GASTRO-ENTERITIS. By K. B. Rogers and others (<i>British Medical Journal</i> , ii, 31st December, 1949, p. 1501) ..	272
ROSS INSTITUTE OF TROPICAL HYGIENE : COURSE IN TROPICAL HYGIENE FOR PLANTERS AND MINERS. TO BE HELD FROM 24TH TO 28TH JULY, 1950 ..	263	TREATMENT OF PULMONARY TUBERCULOSIS WITH PARA-AMINOSALICYLIC ACID AND STREPTOMYCIN (<i>British Medical Journal</i> , ii, 31st December, 1949, p. 1521) ..	272
DRAFT STANDARDS FOR SULPHURIC, HYDROCHLORIC, NITRIC AND BORIC ACIDS ..	263	TREATMENT OF A LUNG ABSCESS BY INHALATION OF MICROPULVERIZED PENICILLIN. By D. T. O'Driscoll (<i>Lancet</i> , ii, 19th November, 1949, p. 945) ..	273
THE USE OF STREPTOMYCIN : REPORT PUBLISHED BY THE EXPERT COMMITTEE OF THE WORLD HEALTH ORGANIZATION ..	263	HYALURONIDASE IN PÆDIATRICS (<i>Lancet</i> , ii, 17th September, 1949, p. 522) ..	273
BRITISH SURGEONS INVITED TO YUGOSLAVIA ..	264	LOW-SALT DIET IN TREATMENT OF HYPERTENSION AND HYPERTENSIVE HEART DISEASE. By H. O. Bang et al. (<i>British Medical Journal</i> , ii, 26th November, 1949, p. 1203) ..	273
THE NEW SURGICAL NYLON DRESSING FOR WOUNDS ..	265	REMISSIONS IN ARTHRITIS (<i>Journal of the American Medical Association</i> , Vol. 141, 12th November, 1949, p. 782) ..	273
		AMOEBIASIS IN INFANCY. By P. C. C. De Silva (<i>British Medical Journal</i> , ii, 26th November, 1949, p. 1208) ..	274

(Continued on page 236)

CONTENTS—(Continued from page 235)

	Page		Page
DRONCORTONE ACETATE AND ASCORBIC ACID IN THE TREATMENT OF RHEUMATOID ARTHRITIS. By D. L. Vay and G. E. Lorton (<i>Lancet</i> , ii, 17th December, 1949, p. 1134)	274	RENAL CALCULUS. By H. P. Winsbury-White (<i>Medical Press</i> , Vol. 222, 5th October, 1949, p. 317)	275
CHLOROMYCETIN IN SCRUB-TYPHUS. By H. McC. Giles and other (<i>Lancet</i> , i, 7th January, 1950, p. 16)	274	CANCER OF THE BREAST (<i>Medical Press</i> , Vol. 223, 4th January, 1950, p. 4)	279
AN UNUSUAL CASE OF SHOPLIFTING (<i>Lancet</i> , ii, 17th December, 1949, p. 1158)	274	BAL AND URANIUM POISONING (<i>Medical Press</i> , Vol. 222, 21st December, 1949, p. 574)	280
PROTRACTED NERVOUS COMPLICATIONS OF TYPHOID FEVER. By G. H. Jennings (<i>Lancet</i> , ii, 31st December, 1949, p. 1218)	275	TOLERATION OF CONTACT LENSES (<i>Medical Press</i> , Vol. 222, 21st December, 1949, p. 575)	280
TREATMENT OF LEPROSY WITH DIAMINODIPHENYL SULPHONE BY MOUTH. By J. Lowe (<i>Lancet</i> , i, 28th January, 1950, p. 145)	275	THORACIC COMPLICATIONS OF AMOEBIASIS (<i>Medical Journal of Australia</i> , Vol. II, 24th December, 1949, p. 920)	280
THE FATE OF THE FORESKIN. By D. Gairdner (<i>British Medical Journal</i> , ii, 24th December, 1949, p. 1433)	276	SIMULATED HOMICIDE (<i>Medical Journal of Australia</i> , Vol. II, 12th November, 1949, p. 722)	280
ARTANE THERAPY FOR PARKINSONISM. By L. J. Doshay and K. Constable (<i>Journal of the American Medical Association</i> , Vol. 140, 27th August, 1949, p. 1317)	276	MULTIPLE AMOEBIC ABSCESS OF THE LUNGS. By P. K. Chatterjee and S. Sen Gupta (<i>Journal of the Indian Medical Association</i> , Vol. 18, September 1949, p. 481)	281
AUREOMYCIN TREATMENT OF AMOEBIASIS (<i>Journal of the American Medical Association</i> , Vol. 140, 27th August, 1949, p. 1344)	276	MOTION SICKNESS (<i>Medical Journal of Australia</i> , Vol. II, 23rd July, 1949, p. 140)	281
AUREOMYCIN AND ALUMINUM HYDROXIDE. By B. A. Waisbr�n and other (<i>Journal of the American Medical Association</i> , Vol. 141, 26th November, 1949, p. 938)	276	STREPTOMYCIN TREATMENT OF OZENA. By K. M. Simonton (<i>Proceedings of the Staff Meetings of the Mayo Clinic</i> , Vol. 24, 8th June, 1949, No. 12, as abstracted in the <i>Journal of the Philippine Medical Association</i> , Vol. 25, August 1949, p. 409)	281
THE EFFECT OF WATER AND SALT INTAKE ON PRICKLY HEAT. By G. O. Horne and R. H. Mole (<i>Lancet</i> , ii, 13th August, 1949, p. 279)	277	AN IMPROVED SWAB FOR THE DETECTION OF THREADWORM OVA (<i>Physician's Bulletin</i> , Vol. 14, November-December 1949, p. 178)	282
TREATMENT OF HERPES ZOSTER WITH AUREOMYCIN. By M. L. Binder and other (<i>Journal of the American Medical Association</i> , Vol. 141, 10th December, 1949, p. 1050)	277	TREATMENT OF GLAUCOMA (<i>Medical Journal of Australia</i> , Vol. I, 14th January, 1950, p. 56)	282
EPILEPSY AS A SEQUELA OF RECURRENT MALARIA. By D. R. Talbot et al. (<i>Journal of the American Medical Association</i> , Vol. 141, 17th December, 1949, p. 1130)	277		
AUREOMYCIN THERAPY IN HUMAN BRUCELLOSIS DUE TO <i>Brucella abortus</i> . By A. I. Braude et al. (<i>Journal of the American Medical Association</i> , Vol. 141, 19th November, 1949, p. 831)	277	REVIEWS	
A SIMPLIFIED CAFFEINE GASTRIC TEST MEAL FOR THE DIAGNOSIS OF PEPTIC ULCER. By V. H. Musick et al. (<i>Journal of the American Medical Association</i> , Vol. 141, 19th November, 1949, p. 839)	278	OBSTETRIC ANALGESIA AND ANÆSTHESIA: THEIR EFFECTS UPON LABOUR AND THE CHILD. By F. F. Snyder, M.D. 1939	282
HOSPITAL OUTBREAK OF ENTERITIS DUE TO DUCK EGGS. By L. P. Garrod and M.B. McIlroy (<i>British Medical Journal</i> , ii, 3rd December, 1949, p. 1259)	278	RECENT ADVANCES IN PHYSIOLOGY. By W. H. Newton. <i>Seventh Edition</i> . 1949	282
		THE RAT IN LABORATORY INVESTIGATION BY A STAFF OF TWENTY-NINE CONTRIBUTORS. Edited by Edmond J. Farris, Ph.D., and John Q. Griffith, Jr., M.D. <i>Second Edition</i> . 1949	283
		NORMAL VALUES IN CLINICAL MEDICINE. By F. William Sunderman, M.D., Ph.D., and Frederick Boerner, V.M.D. 1949	283
		PRINCIPLES OF MEDICAL STATISTICS. By A. Bradford Hill, D.Sc., Ph.D. <i>Fifth Edition, Revised and Enlarged</i> . 1950	283
		CORRESPONDENCE	
		PENICILLIN TREATMENT OF GLYCERINE VACCINE LYMPH	283
		A NOTE ON FILING MEDICAL JOURNALS	284
		PRECAUTIONARY MEASURES IN THE MANAGEMENT OF PNEUMONIC PLAGUE	284

Original Articles

OUTBREAK OF KALA-AZAR IN AN INSTITUTION IN BOMBAY

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(Acworth Leper Home, Matunga, Bombay)

THIS communication reports the study of an outbreak of kala-azar in an institution in Bombay. The first part describes the outbreak as it manifested itself; the second part details the investigations carried out to determine (a) the origin and the spread of the outbreak, and (b) if an endemic focus of kala-azar existed in Bombay.

Detection of the outbreak

All the patients came from the Acworth Leper Home, Bombay. This home has a shifting population of some 400 inmates at a time. It is meant to cater for persons suffering from leprosy in the Province of Bombay, but a census taken at any time will disclose a goodly number drawn from other provinces, especially from the Province of Madras and Madhya Pradesh. Unless bedridden the inmates can mix with one another freely.

Whenever possible, all the bodies from the Acworth Leper Home are submitted for autopsy to the Department of Pathology and Bacteriology, G. S. Medical College. The first indication of the outbreak of kala-azar among the inmates of the Home was given by the unusual finding that two bodies examined during the course of a single week showed the presence of kala-azar, in addition to leprosy. Recalling that in Bombay in a big general hospital like the King Edward VII Memorial Hospital with a total average admission rate of over 20,000 per annum there are at the most 6 to 10 cases of kala-azar (almost all 'imported') in the whole year, the detection of 2 cases of kala-azar at autopsy during the course of a single week and in patients coming from the same source naturally aroused the suspicion of a possible outbreak.

Detection of cases

Three procedures were adopted to ensure the detection of every case in the suspected outbreak. (1) Every case of leprosy that came for

autopsy subsequent to the above two cases was investigated critically to find out if there was coincident kala-azar as well. This entailed examining the splenic smears and sections of the liver and the spleen for the presence of the Leishman-Donovan bodies. By this means up to date we have discovered 9 cases of kala-azar among the autopsies performed on patients from the Acworth Leper Home between February 1949 and March 1950. (2) All the previous autopsy material from the Acworth Leper Home was re-examined in order to find out whether we had missed some earlier cases—missed, because the possibility of kala-azar was not in mind and, therefore, the material was not examined specially for the parasite. This revealed 3 more cases; these cases were missed because the splenic enlargement was inconspicuous, splenic smears were not examined, and sections of the liver and the spleen were not searched with the oil-immersion lens. (3) The number of positive cases obtained by the above two procedures led us to believe that among the inmates of the Home there must be some more cases of kala-azar. It was not possible to investigate every one of the 400 inmates by either a sternal marrow biopsy or a splenic puncture. We, therefore, adopted the practical plan of examining the sternal marrow, by microscopy and cultural examination, of all the patients whose sera gave a positive aldehyde test. Out of 454 patients on whom the test was done 40 gave a positive reaction, 17 being strongly positive and 23 weakly positive (see Napier, 1943, for interpretation of the test); and, of the positives, 8 were proved to be suffering from kala-azar. In all these patients the Leishman-Donovan bodies were present in the smears of the sternal marrow, and the leptomonas were grown in culture on the N.N.N. medium. The patients diagnosed during their life-time were treated for kala-azar. One of them died later, while the others are still living.

The results of the above investigations are summarized in table I. In all there were 20 cases of kala-azar in the Acworth Leper Home. The first case was detected on 23rd April, 1948, and the latest—it may not be the last—on 14th October, 1949.

Investigation of the outbreak

The occurrence of such a large number of cases in a single institution within a short space of time was itself very suggestive of a local outbreak and could not possibly be a mere chance accumulation of imported material. However, in the investigations undertaken, an effort was made to secure positive proof for this. The findings in this connection may be summarized as follows:

1. *Evidence from the patients' clinical history.*—The case records of every positive case were analysed with a view to finding out (a) the place from which the patient came and

TABLE I

Number of bodies from the Acworth Leper Home autopsied during the period of investigation	Cases of kala-azar	RESULTS OF ALDEHYDE TESTS				Cases of kala-azar
		Total number of aldehyde tests	Negative	Weakly positive	Strongly positive	
38	12	454	414	23	17	8

(b) the duration of his stay in Bombay. It was noticed that calculation of the patients' stay in Bombay from the total period of their segregation in the Home was misleading, because some of them had absconded from the Home on one or more occasions after their first admission. The period of their definite uninterrupted stay in Bombay was, therefore, calculated from the date of the last re-admission to the date on which death occurred, or, in the case of patients still alive, up to the day of definite diagnosis. The data so obtained are presented in table II. The figures, be it noted, indicate the minimum duration of these patients' stay in Bombay. The table shows that 6 of the patients (starred items) had stayed in Bombay uninterruptedly for at least 3 years, and in the case of 1 of these this period was 13 years. The figures for the minimum interrupted stay in Bombay were

further related to the figures for the incubation period of kala-azar. This is generally assumed to be 2 to 4 months, the widest range being from 10 days to 2 years. Thus it appeared that 6 of the patients, with at least 3 years of uninterrupted stay in the Home, were almost certainly infected in the Home. Here, then, was strong evidence to show that the whole outbreak was of local origin.

2. *Demonstration of the presence of sand-flies in the affected locality.*—Controversy still rages round the possible insect-vector of kala-azar as well as the mode of infection in the disease. All the positive proof available, however, points to the sand-fly as the insect-vector, and further, that it transmits the infection by its bite. We, therefore, attempted to find out if sand-flies existed in the compound of the Acworth Leper Home. The Home has a large

TABLE II

Serial number	Native place	Date of first admission	Date of the last re-admission	Died on	PERIOD OF UNINTERRUPTED STAY IN BOMBAY AS CALCULATED FROM THE DATE OF LAST RE-ADMISSION TO DATE OF DEATH OR UP TO THE DAY OF DEFINITE DIAGNOSIS		
					Years	Months	Days
1	Nasik Dist. (Yeole)	7-3-46	7-10-47	Living	1	9	3
2	Satara Dist. (Sakurda)	19-5-48	Never absconded.	"	1	1	21
*3	Thana Dist. (Ulthan)	20-3-45	"	"	4	3	11
*4	Bangalore	21-6-44	"	"	5	..	19
*5	Ratnagiri (Savarda)	19-6-42	8-2-43	"	6	5	2
6	Mahim, Bombay	18-2-47	Never absconded.	"	2	7	26
7	Alibag (Colaba)	8-5-45	"	"	1	5	6
8	Madras	4-3-48	26-1-49	14-4-49	..	2	20
9	Madras	8-5-48	1-3-49	2-4-49	..	1	2
10	Madras	23-8-47	18-2-48	23-3-49	1	1	6
*11	Ratnagiri (Sangameshwar)	2-12-43	1-2-45	5-8-48	3	6	5
12	Ratnagiri (Malwan)	1-10-38	2-1-48	6-5-48	..	4	5
13	Colaba Dist. (Mangood)	10-11-38	10-10-47	22-4-48	..	6	13
*14	Goa (Kolwal)	21-10-35	Never absconded.	16-2-49	13	3	27
15	Ratnagiri (Ratnatan)	13-10-45	29-9-48	1-3-49	..	5	..
16	"	4-3-48	8-12-48	4-3-49	..	2	25
17	Bangalore	25-5-48	17-5-49	28-5-49	12
18	Nagpur	2-10-43	28-3-49	27-5-49	..	2	..
19	East Khandesh (Jalgaon)	31-3-43	9-6-47	6-10-49	2	3	27
*20	Colaba (Alibag)	6-1-44	Never absconded.	20-11-49	5	10	14

compound with many trees, plenty of shrubbery, and a vegetable garden. There are no cattle sheds or live-stock in the compound or in the vicinity of the Home. Most of the roads within the compound are neither metalled nor cemented, and small stagnant collections of water can occur near the wards. The latter, for the most part, are of the nature of hutments to accommodate some 20 to 30 patients in each. The roofs and the walls of the hutments show many dark corners and cracks. The place appeared to be well-suited for the breeding of sand-flies.

By means of 'light-traps' over 1,100 'flies' of all kinds were trapped and examined. Among them were 47 sand-flies (33 males and 14 females). It may be recalled that Sinton (1927), and Young and Chalam (1927) have previously recorded the presence of many species of sand-flies (including *P. argentipes*) in the City of Bombay. No information, however, is available on the prevalence and the distribution of sand-flies in Bombay at the present day. The insect-vector proved responsible for the transmission of the disease from one patient to another was demonstrated to be present in the locality affected.*

(3) *Presence of sand-flies infected with Leishmania donovani.*—With the exception of a few mounted as permanent specimens every sand-fly that was caught was dissected and smears were prepared from the material obtained by crushing the pharynx and the mid-gut. The smears were stained with the Leishman or the Giemsa stain and searched carefully for the presence of *L. donovani*. Up to now we have been able to demonstrate at least 5 female sand-flies infected with *L. donovani*. In the smears studied we could see various developmental stages of the parasites from the typical Leishman-Donovan bodies to the leptomonad form (Bhende *et al.*, 1949). Morphologically these forms appear identical with those seen in human material. We did not make cultures of the material from sand-flies.

Comment

In a previous paper (Bhende *et al.*, *loc. cit.*) we have discussed in detail the implications of the above findings. The additional data gathered since support all the conclusions drawn previously. These latter may be briefly reiterated as follows: (1) In the outbreak investigated the primary source of infection could only be human. (2) When and how exactly was the infection introduced in the Home could not be stated definitely, but probably the infection was brought by some of the inmates who came from Madras—a heavy endemic focus of kala-azar. (3) The sand-flies existing in the compound of the Home caught the infection and transmitted it to new hosts. (4) Due to the diminished

resistance of the patients suffering from leprosy such transmission was facilitated.

It would appear that a reservoir of kala-azar cases has been built up in Bombay. And, with the presence of the insect-vector in the vicinity, it can serve as an endemic focus for disseminating the infection to the general population of the city. That such a spread has actually occurred either from this or some other hidden foci is evidenced by the recent reports of undoubted indigenous cases of kala-azar (Row and Patkar, 1947; Raghavan, 1949).

Summary

1. An outbreak of kala-azar in the Aeworth Leper Home, Bombay, is described. In all 20 cases were encountered: 12 were diagnosed at the autopsy and 8 in living patients.
2. The comparison of the figures for those persons' uninterrupted stay in the Home with the incubation period of kala-azar showed that some of the patients were certainly infected locally.
3. The insect-vector—sand-fly—was demonstrated to be present in the compound of the Aeworth Leper Home.
4. Some of the sand-flies caught were shown to be infected with the Leishman-Donovan bodies.
5. It is pointed out these cases may serve as an endemic focus for spreading the infection to the general population of Bombay.

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TUMOURS OF ENDOTHELIAL ORIGIN

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THIS large group of neoplastic tumours arises from the cells lining the blood vessels, lymph vessels and spaces, sub-dural spaces and serous

* The sand-flies are being studied further to identify the species to which they belong.

cavities. The history of development of the present state of our knowledge of this group of tumours is full of controversies, incompleteness and confusion. Kettle (1925) observed that 'in entering upon a description of the tumours derived from endothelium we are confronted with quite exceptional difficulties for in respect to no other class of neoplasms is there so much divergence of opinion'. Harvey and others (1940) in their discussion on debatable tumours remark about this group of neoplasms that 'the use of the term endothelioma, not merely for purposes of discussion but as an accredited tumour, may seem a retrograde step, considering the extent to which the term has been condemned by disuse and disapproval. Our study on the question, however, has convinced us that

both morphologically and embryologically the term can logically be used for a definite tumour group which otherwise lacks unity of interpretation'. Ewing (1948) wrote an exhaustive and admirable discussion on the physiological and biological placing of the endothelium and pointed out the dual rôle of the endothelium as epithelial and connective tissue. He produced the following histological types of the endothelial tumours :—

- (1) Perivascular.
- (2) Adenoid.
- (3) Angio-endothelioma.
- (4) Diffuse endotheliomata.

Willis (1948) challenged and put forward strong arguments against the histological entity

Endotheliomata—125 cases

TABLE I

Age	Number of cases
1-10	7
10-20	20
20-30	23
30-40	25
40-50	23
50-60	13
60-70 and onwards	1
Age unrecorded	13
TOTAL	125

TABLE II

Sex	Number of cases
Male	69
Female	47
Sex unrecorded	9
TOTAL	125

TABLE IV

Histological types according to Ewing's classification

Types	Number of cases
A. Perivascular perithelioma	10
B. Adenoid	9
C. Angio-endothelioma—	
Hæmangio-endothelioma	18
Lymphangio-endothelioma	14
Undifferentiated	5
D. Diffuse synovioma	1
E. Unclassified—	
Diffuse arrangement of cells, endothelial in appearance, not fitting with any of the above patterns.	68
TOTAL	125

TABLE III

Site of origin

Region	Number of cases
(1) Scalp	3
(2) Vertex of head	1
(3) Forehead	2
(4) Back of head and occipital region	2
(5) Antrum of Highmore	1
(6) Left temporal region	1
(7) Region of orbit, eyeball and ethmoid	8
(8) Nose	9
(9) Mouth (floor 2, palate 6, angle of mouth 1, tongue 1).	10
(10) Lips	4
(11) Pharynx and nasopharynx	3
(12) Neck	4
(13) Mandible	1
(14) Region of jaw	1
(15) In front of left external and auditory meatus.	1
(16) Cheek	4
(17) Axilla, scapula, deltoid region	3
(18) Brain	1
(19) Thyroid	1
(20) Small intestine	1
(21) Large intestine	2
(22) Cæcum	1
(23) Omentum	1
(24) Retroperitoneal region	1
(25) Medial to left clavicle	1
(26) Chest wall	2
(27) Forearm	5
(28) Broad ligament	1
(29) Uterus (cervix 6, body 4)	10
(30) Ovary	5
(31) Bones (humerus 1, femur 1, frontal 1, tibia and fibula 1).	4
(32) Artery (popliteal)	1
(33) Thigh	1
(34) Scrotum	2
(35) Breast	1
(36) Vagina	1
(37) Recto-vaginal septum	2
(38) Knee	3
(39) Glands—	
Cervical	1
Femoral	1
Inguinal	1
Preauricular	1
Near elbow joint	12
(40) Region unrecorded	1
TOTAL	125

as endothelioma and finally observed 'that for well differentiated growths of the mesenchymal tissues which happen to possess surfaces we already have adequate distinctive names, and that for poorly differentiated sarcomatous growths of these tissues the name "endothelioma" is still unnecessary and in view of what we know of the plasticity of the multiple mesenchymal cells inappropriate'. Hastings-James (1949) discussed the points raised by Willis with regard to the pathological entity of the angiomatous tumour and described one such tumour which originated from the hepatic structure and described it as 'hamangioblastoma of liver'. So long as the aetiology of neoplastic tumours and the complete understanding of the biological relationship of different tissues are not worked out, the divergence of opinion will continue to exist. More knowledge of essential to clear up these controversies. On going through our records for the last twenty years we find that altogether we have reported 125 cases as tumours of this origin. We are giving in short the summary of these cases (see tables I to IV) and describing in detail the four recent cases that we have come across.

Case 1

Clinical notes.—European male, aged 44 years, history of gradual loss of weight since February 1941 with weakness and malaise. In April 1941 enlargement of the abdomen was noticed which led to paracentesis in June. There was no enlargement of the liver or jaundice and the fluid drawn was highly albuminous. Tapping was repeated on several occasions at intervals of 2 weeks or so till August when the fluid drawn was found to be blood-stained. There was no general anasarca at any time, no cardiac sign or hepatic deficiency nor could there be found any evidence of intestinal growth. The abdomen was opened on 23rd August and an omental tumour like grapes in appearance was removed. Since removal there has been a steady improvement under deep x-ray treatment and there has been but one tapping. The patient continued making good progress and gained in weight. Four years after he was found enjoying good health and continuing his usual work.

Naked eye examination.—The omental tissue was studded with cystic growths and solid greyish white tumour nodules of different sizes. The big cysts were of the size of a marble and the small ones were smaller than peas. The cystic growths were seen to be connected with the solid tumour masses. The cyst contained thin gelatinous material (figure 1, plate XXXVI).

Histology.—Sections from one of the small nodules (figure 2, plate XXXVII) showed collection of empty tubular spaces lined with endothelial type of cells; at certain areas these endothelial cells showed proliferative changes forming clusters of cells. Sections from the bigger nodules (figure 3, plate XXXVII)

showed almost complete absence of empty tubular spaces but a compact mass of cells showing the characteristics of embryonic nature and plenty of mitosis. Sections from the cysts showed quite a different picture (figure 4, plate XXXVII), viz, large cystic spaces containing structureless material, possibly coagulated lymph. In some of the cysts the lining walls had undergone much thinning due to pressure.

Comments.—The origin of the tumour is obviously from the endothelial lining of the peritoneal lymphatics. We find two types of changes—one forming solid nodules and the other cysts. The bigger nodular areas show characteristics of a malignant tumour formation (figure 3, plate XXXVII). The other change, viz, the cyst formation, is a well-known phenomenon of the endothelial tumour of peritoneal origin.

The patient was found quite fit for four years after the operation. This goes against the high malignancy of the tumour. The deep x-ray therapy also might have been responsible for the non-recurrence or further spread. When the abdomen was opened this mass protruded and was cut and the abdomen was closed. So the possibility of other foci remaining inside was there, and how far the deep x-ray could reach the remnant of the tumour is a matter of conjecture. The possibility of a low and locally malignant nature of the tumour can also be thought of.

A case of large epigastric endothelioma possibly of lymphatic origin, growing between the layers of the great omentum, causing acute retention of urine by being impacted in the pelvis, has recently been recorded by Guthkeleh (1948). His specimen also showed both firm and cystic areas though not so conspicuously as in our case. The Pathologist (Professor S. L. Baker of Manchester University) opined in the case of Guthkeleh thus: 'It is difficult to assess the grade of malignancy; cytologically it is not highly malignant, but would no doubt recur locally if not completely removed'. Although a few tiny transparent cysts were seen scattered over the remainder of the great omentum and in the pouch of Douglas, the patient was free from recurrence and was at work and in normal health 4 years after the operation, without any post-operative treatment.

Case 2

A. J. C., Indian, aged 60 years, a retired School Inspector, was admitted into the hospital for swelling and pain in the right arm. About a year and a half before his admission he first felt pain in the arm which was intermittent in nature. Within a few weeks of the onset of the pain he noticed that the arm got swollen at the upper part. Subsequently he injured the same arm and his forearm got flexed at right angles to the arm. According to him this was due to the trauma that he sustained. The swelling gradually increased. On examination a large

swelling extending over the lower two-thirds of the right arm was seen. The tumour was reddish in colour and there were prominent veins over it. The head of the humerus seemed to be dragged out of the socket. Above the main swelling there was another small swelling which was softer in consistency than the main swelling. The forearm was found to be thinner than its fellow, the patient could move his fingers and hand. The main swelling was hard, irregular, tender and pulsating. At certain areas egg-shell crackling could be elicited. A skiagram was taken (figure 5, plate XXXVII) and the following was seen. The whole of the bone was involved in a fusiform swelling. In place of normal osseous structure there were a number of thin bony lines forming several compartments. The bony outline of the humerus was lost. A provisional diagnosis of osteoclastoma was made. The arm was amputated. A sagittal section of the tumour was made which showed the following (figure 6, plate XXXVI). The tumour was composed of fleshy masses which were found to be in several compartments which were outlined by thin bones. These areas were of different colours—some deep red, others dull red, chocolate and pale cream. The tumour process ended rather abruptly. The microscopic picture was studied from different portions of the tumour mass and showed the following structural patterns. Certain areas were composed of large cubical or cylindrical cells arranged in cords or columns. The cells were large with clear cytoplasm, sharp cell membrane and small nucleus (figure 7, plate XXXVII). The appearance here was very similar to a picture produced by Ewing (1940). In other areas, the picture was dominated by the presence of large cystic spaces filled with blood (figure 8, plate XXXVIII). The cyst-like blood spaces were found to be lined with a fine layer of connective tissue but had no lining endothelial cells. In others, there was scarcity of such blood spaces but there were collections of groups of cells scattered without any definite arrangement (figure 9, plate XXXVIII). These large blood spaces and collections of groups of cells formed the main picture of the most dark red areas whereas the pale areas were mainly composed of material depicted in figure 3, plate XXXVII. The patient got well and was discharged from the hospital. Six months after his discharge he died of a febrile condition.

Comments.—According to Ewing's contention this case has been labelled as hæmangioma of the bone. Willis (1948), however, opined thus: 'No modern pathologist should be so misled by finding blood within adenocarcinomatous spaces that he mistakes renal or other carcinoma for "hæmangio-endothelioma" as was once done; yet as Stont points out the last edition of Ewing's textbook (1940) contains an illustration labelled "angio-endothelioma of bone" which almost certainly perpetuates this old error and Thomas has made a similar mistake'. So the

question arises whether this case should be described as a carcinoma, a hæmangio-endothelioma or a sarcoma. During the patient's stay in the hospital there was no suspicion of any primary growth anywhere else but in the absence of a complete post mortem this question cannot certainly be ruled out. Willis raises the question about the degree of vascularity which will decide whether a particular growth should be an angioma or a vascular carcinoma or sarcoma. In this case the points are in favour of an angiomatous condition. The large blood spaces (figure 9, plate XXXVIII) lined without the endothelial layer and the presence of cluster of cells without any arrangement (figure 5, plate XXXVII) may be explained by the fact that from the developmental point of view the endothelium and the red blood cells have different origins. So it is possible that in the course of atypical formation of the growth these two elements have been separated. Though rare, this tumour has been found in other bones as well. A fair number has been recorded in the vertebræ by Schmorl (1932) and Ghormley and Adson (1941), majority of which had no clinical symptoms. Radiologically some of these vertebral tumours presented similar appearance as our case, i.e. 'ballooning of vertebral body' with typical honeycombed rarefaction, which may lead to collapse and wedging. Those of the long bones give a characteristic, loose, soap-bubble appearance, and longstanding lesions may cause extensive destruction and pathological fracture.

Case 3

A. L., male, aged 25 years, occupation, sweeper, admitted into the hospital on 18th September, 1948.

Complaints.—Pain and vomiting after taking food, duration 1 year.

History of the illness.—The patient used to get irregular colicky pain in the upper abdomen (epigastrium) about 1½ years back. During the last one year, pain increased and the patient used to vomit intermittently. The vomited matter was of foul odour and sour in taste and contained food material 3 to 4 days old. The patient had black coloured stool 3 to 4 times during the period (not definitely tarry). He noticed a lump in the abdomen for 1 year. He gave past history of dysentery.

On examination.—The patient was found to be considerably wasted. Heart, lungs, liver, spleen, no abnormality. P/R, 80/20 per minute. Temperature, normal. Tongue, coated and moist. Teeth and gums, unhealthy.

Locally, abdomen soft, moving with respiration. Visible peristalsis from left to right was seen in the hypogastrium and lower part of umbilical region on taking food or water. No lump felt in the abdomen. Three days after admission, patient had dental trouble for which 3 teeth were extracted.

Results of investigation: Barium meal examination of gastro-intestinal tract showed obstructive dilatation of stomach. Gastric analysis showed no significant findings.

Clinical diagnosis of pyloric stenosis was made.

Operation done on 17th October, 1948. Anaesthesia, intercostal block and local novocaine infiltration.

Abdomen was opened by right paramedian incision. Some air-containing cystic tissue was found occupying the space between the anterior surface of the liver and the diaphragm as well as the subhepatic region. On exploration it was considered to be composed of pneumatic cysts on the serous surface of the small intestine. The cysts were present from 4 inches of the ileocaecal junction to about 2 feet from the junction. One cyst was present on the caecum. The stomach was considerably dilated with thickening of the pyloric region with no obvious evidence of ulceration. Resection of 20 inches of affected small intestine with end to end anastomosis was done. A posterior retrocolic, isoperistaltic gastrojejunostomy was also done. Abdomen was closed in layers. Post operative: The patient was given small milk feeds 2-hourly from 48 hours after operation.

On 22nd October, 1948, the patient was having frequent loose motions for which sulphaguanidine was given and loose motion stopped. He made an uneventful recovery although he complained of a little distension of the upper abdomen due to taking of a larger quantity of solid food at a time secretly than was prescribed. By taking smaller quantity more frequently this discomfort passed off.

On 23rd November, 1948, barium meal examination showed stomach functioning and still dilated.

On examination of the peritoneal surface of the specimen (figures 10a, plate XXXVIII, and 10b, plate XXXVI) numerous cysts of different sizes could be seen. This specimen differed from that of case 1 in having no hard nodules. The cysts were of different consistency. Some felt hard but on cutting open they were found to be cystic. The walls of these were definitely thicker than those of the softer cysts. Histological sections were made from both types of cysts, soft and hard, from different portions of the specimens. Section from the wall of the hard cystic areas (figure 11, plate XXXVIII) showed numerous blood vessels of different sizes stuffed with red blood cells. The histological appearance of the case was different from that of case 1. In this case no purely cellular areas could be found. All the sections that were studied from the comparatively hard cysts showed the presence of a very large number of young capillaries. Sections from the soft and thin cysts showed large empty spaces containing thin mucinous material (figure 12, plate XXXIX). At the base of these cystic spaces numerous capillaries could be found.

Comments.—So far as the multiple cysts are concerned this case was similar to case 1 but in other features it differed. In this case no purely cellular areas could be found. The study of all the sections that were made from the comparatively hard cysts showed only numerous capillaries. These hard cysts were so numerous that a malignant angiomatous process was to be suspected. Following even Willis' contentions this picture cannot be explained as merely a state of increased vascularity in a malignant tumour of connective tissue or epithelial origin. These tumours may occur in practically any tissue of the body. Recently an angio-endothelioma in the gluteal muscles (a rare site) has been recorded by Ewing (1948). Numerous similar cases were collected from the literature by Shallow, Eger and Wagner (1944). In the majority, the tumour is wholly or partially diffusely infiltrating. Although the infiltrating characteristics of the diffuse type suggest potential malignancy, metastasis occur in less than 1 per cent of cases (Geschickter and Kearsbey, 1935).

'They are probably congenital tumours, due primarily to an incomplete maturation of some of the elements in the developing vascular tree' (Ewing).

One year after the operation the patient was doing his usual work.

Case 4

R. P., female, aged 22 years, admitted into the hospital on 4th May, 1948.

Complaints.—(1) Swelling in the left axilla and scapular region, duration 1 year. (2) Pain in the swelling, 15 days.

History of the illness.—About 3 years ago, the patient developed a fleshy swelling over the left scapula, which increased to 3 inches in diameter in course of a year. She was operated upon elsewhere and the growth was removed. For 1 year after the operation, she was well without any lump. During the last year, a swelling reappeared in the same region and has been increasing rapidly in size. Formerly, she used to feel intermittent pain in the swelling, but for the last 15 days, she has been feeling marked pain continuously in the swelling. For the last 1 month, the swelling has been hot and red in colour. No history of fever, hæmoptysis or pain in the chest.

On examination, patient moderately anæmic. Heart, lungs, liver and spleen, no abnormality. Locally, a sessile irregular swelling about 6 inches in diameter extending from the left anterior axillary fold to the scapular region, consistency firm, no fluctuation, margin fairly well defined, adherent to skin, mobility over the scapula doubtful. Swelling not compressible. Superficial veins prominent. Movements of the shoulder joint normal but for the mechanical

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PNEUMOCOCCAL MENINGITIS WITH

ATYPICAL FEATURES
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When meningitis is suspected we look for signs of meningeal irritation. Great importance is naturally placed on neck rigidity and positive

Kernig's sign. If they are present we proceed to do a lumbar puncture. In their absence it is often argued that it could not be a case of

meningitis as there were no neck rigidity and positive Kernig's sign. In most cases the conclusion may be right. But the following cases suggest that negative Kernig's sign and absence

of meek rigidity, do not always invalidate the diagnosis of meningitis. Those signs depend on the degree of irritation of the meninges, hence

the period of separation and initial stages of development, the period of development and the period of production of the product.

Moreover, in cases where shock is a prominent feature, either due to toxæmia or adrenal cortical involvement, or coma is pronounced due to the metabolic disturbance.

to the main point of the disease falling on the brain the above signs may be absent. Further those are the signs where personal factors count at least in the early stage of the disease.

is by examination of the cerebrospinal fluid, and that the prognosis in meningitis depends mainly on the early stage of the disease.

on the promptness of the institution of special treatment. Hence it is suggested that absence of neck rigidity or negative Kernig's sign should

not prevent one from making a lumbar puncture in cases of suspected meningitis. It should also be noted that in the fulminating type meningitis producing adrenal crisis

phalitic syndrome or mixed encephalitic-adrenal phalitic syndrome (Banks and McCartney, 1943) there may be no neck rigidity or Kernig's sign.

block due to the swelling (figure 13, plate XXXIX).

A clinical diagnosis of fibrosarcoma was made. X-ray (figure 14, plate XXXIX) showed some osseous tissue in the growth of the soft parts. The axillary border of the scapula was somewhat irregular. Radiological diagnosis was fibrosarcoma.

X-ray of lungs showed no evidence of metastasis. Calcified lymph nodes in the hilar regions.

Operation done on 13th May, 1948. Anaes-

thesia, rectal paraldehyde with gas and oxygen. A longitudinal incision parallel to 3rd part of axillary artery was made in the left axilla and the growth carefully dissected off important vessels and nerves of the axilla. The incision was extended inwards along the anterior axillary fold, and the dissection further proceeded with in the axilla. A solid band slightly darker in colour than a muscle, rectangular in cross section with the corners rounded off, extending from the lower part of the growth at the inferior angle of the scapula and gradually tapering towards the axillar vessels, was found. It appeared as an accessory slip of muscle. This structure was clamped and divided between clamps. (After cutting, it was found to be a vein filled with solid material which was found to be dirty white in colour. Later it was found to be the subscapular vein, solidly packed with extension of growth.)

The incision was continued around the upper part of the axillary order of the scapula, the scapular circumflex was found to be dilated and solid. It was divided, and the contents showed yellowish-white solid material (extension of growth). The growth was loosely adherent to articular capsule of shoulder, from which it was dissected without difficulty. Muscles arising from the axillary border of scapula were divided and the growth removed. The axillary border of the scapula was snipped off with bone cutting forceps as it was found rough and bare. As the skin was short to cover the wound, the arm was fixed to the side of the chest by making skin flaps in both and suturing them. Patient had blood and plasma transfusion to tide over the operative shock.

The patient became very boisterous and unconscious, with high temperature of 103°F. to 104°F. which persisted for 3 days, in spite of every kind of sedative including repeated doses of morphia and high doses of penicillin. Lungs were found to be clear, no localizing neurological signs. Blood count showed marked leucocytosis. Total W.B.C. 25,900, polymorphs 91 per cent. No hæmoptysis. Clinically, the condition resembled acute encephalitis. Lumbar puncture showed clear fluid under tension. The patient died on 16th May, 1948. Her husband refused post-mortem examination.

Summary and conclusions

1. One hundred and twenty-five cases of tumour believed to be of endothelial origin are reported.
2. Four recent cases of such tumour are described in full.

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Tumours which are situated in areas where normally synovial tissues do not exist, such as middle of thigh or arm, are not suspected as synoviomia until after the histological examination of the tumour. Usually these tumours present two histological patterns: (a) diffuse cellular type and (b) cystic and papillary formations giving the appearance of a pseudo-epithelial papillary adenocarcinoma. The histological appearance of this tumour appears to fall on the second type because the *pseudo-alveolar* appearance was the dominant feature. The terminal signs of encephalitis are probably due to showers of metastasis in the brain, from clamping of the infiltrated vein.

The tumour in the case referred to was loosely attached to the articular capsule of shoulder joint.

These tumours seldom form within the cavities of the joints, instead they lie in close proximity to tendons, tendon sheaths, and outer walls of bursæ or joint capsules.

The tumour in the case referred to was loosely attached to the articular capsule of shoulder joint. The tumour in the case referred to was loosely attached to the articular capsule of shoulder joint. The tumour in the case referred to was loosely attached to the articular capsule of shoulder joint.

Comments.—This tumour was evidently a synoviomia which Willis describes as synovial sarcoma. The widespread distribution of synovial tissues in the body and their possible development from other mesenchymal tissues, when appropriately stimulated, such as adventitious bursa and inner lining of a pseudoarthrosis, etc., undoubtedly explain the occurrence of a synoviomia in areas which are well away from articulations.

extension of the tumour process within it. histological examination found to contain an solid material (figure 17, plate XL) was on The vein which was found to be blocked with to be due to mucoid degeneration in the tumour. The homogeneous slate coloured areas were found pseudo-alveolar form (figure 16, plate XL). many areas these cells were seen taking a brownish areas showed spindle-shaped cells. In blocks from different portions of the several the growth. Histological studies of the several calcarious areas were found scattered through slaty in colour, quite different in appearance from irregular, pale brownish in colour excepting two areas which appeared to be homogeneous, pale and XXXVI the inner surface was found to be On cutting open the tumour (figure 15, plate

pupils were equal and reacted well to light. On admission a lumbar puncture was done. The cerebrospinal fluid was clear and came out under slightly increased pressure. No chemical or bacteriological examination of the fluid was done. Blood : Hb. 80 per cent (Sahli), leucocytes 4,000 per c.mm., polymorphonuclear cells 66 per cent, lymphocytes 30 per cent, monocytes 3 per cent, eosinophils 1 per cent, malarial parasites none found.

On the day of admission he had an intramuscular injection of 10 grains of quinine sulphate and was put on paludrine 0.3 gm. tablets, three times a day for two days. On 15th December, 1949, he was semi-conscious and irritable and remained curled up on one side covered under a blanket. He did not like to be disturbed. The neck was soft and Kernig's sign was negative. Temperature varied between 102°F. and 103°F. On 19th December, 1949, the restlessness increased and he became violent. He severely resented any examination. The clinical picture suggested meningeal irritation. But as the neck was soft, Kernig's sign negative and previous lumbar puncture had revealed normal fluid, the procedure was not repeated. An intramuscular injection of 3 cc. of paraldehyde kept him quiet for a few hours.

On the next day the restlessness was pronounced but the neck was still soft and Kernig's sign negative. An injection of morphine sulph grain $\frac{1}{8}$ had to be given to make the patient quiet.

On 21st December, 1949, in spite of the neck being soft, Kernig's sign being negative, negative report of previous lumbar puncture and absence of leucocytosis in first blood examination, the clinical picture of the patient (semi-consciousness, restlessness, typical decubitus and marked resentment against any examination) was so typical of meningitis, that a lumbar puncture was done again. The fluid was hazy but not under increased pressure. It contained 12 cells per c.mm. mainly of polymorphonuclear type and Gram-positive diplococci. Blood showed 17,400 leucocytes per c.mm., polymorphonuclear cells 78 per cent, lymphocytes 20 per cent, monocytes 1 per cent, and eosinophils 1 per cent. Temperature was 102.8°F., pulse 140, and respiration 30 per minute. Penicillin was given 10,000 units dissolved in 10 cc. normal saline intrathecally and 100,000 units intramuscularly every three hours. He was put on sulphadiazine 1 gm. every four hours. Intrathecal and intramuscular penicillin injections were continued for the next two days in same doses. Temperature came down to normal on 22nd December, 1949, and the patient looked much better. On 24th December, however, it rose again to 102°F. and the patient ran a temperature varying between 98°F. and 102°F. for another 12 days. During this period he had no toxæmia and was perfectly conscious. The tongue was clean and moist, neck was soft, Kernig's sign was negative and

the lungs were clear. He, even with the temperature of 102°F., enjoyed his diet.

Intramuscular penicillin was continued for 10 days and sulphadiazine for 14 days, the dose of the latter drug was later diminished to 0.5 gm. four-hourly.

On 31st December, 1949, blood examination showed 8,600 leucocytes per c.mm., polymorphonuclear cells 76 per cent, lymphocytes 22 per cent, monocytes nil, and eosinophils 2 per cent. Urine was alkaline in reaction and contained plenty of pus cells. On 2nd January, 1950, he was put on hexamine and had injections of glucose 25 per cent 25 cc. with hexamine, 40 per cent 5 cc. on 4th and 5th January, 1950. The temperature came down to normal on 5th January, 1950, and has remained so since then.

Case 3

R. D., male, aged 14 years, was admitted on 28th December, 1949, with history of continued fever for four days and loose motions 8 to 10 times in 24 hours for two days. The onset was with chill, rigor and vomiting. The patient was toxæmic, delirious and markedly dehydrated. Temperature was 104°F., pulse 120, and respirations 24 per minute. No abnormality was detected in heart or lungs. Liver and spleen were not palpable. Neck was soft and Kernig's sign was negative. No abnormality was detected in the nervous system. Lumbar puncture was done. 8 cc. of clear fluid came out under normal tension. It contained 3 cells per c.mm., all lymphocytes. Blood : Hb. 90 per cent (Sahli), leucocytes 24,000 per c.mm., polymorphonuclear cells 86 per cent, lymphocytes 10 per cent, monocytes 2 per cent, eosinophils 2 per cent, malarial parasites nil.

He was put on sulphadiazine 1 gm. four-hourly. Normal saline with 5 per cent glucose was given subcutaneously for dehydration.

On 29th December, 1949, the temperature came down to 99°F. in the morning but again went up to 103°F. towards the evening. The neck was slightly stiff and Kernig's sign slightly positive. On lumbar puncture 10 cc. of clear fluid under normal tension were drawn. Suspecting it to be a case of meningitis, 10,000 units of penicillin dissolved in 10 cc. normal saline were given intrathecally. Subcutaneous saline was repeated. On 30th December, the lumbar puncture was repeated and 18 cc. of hazy fluid were drawn under slightly increased pressure. The cerebrospinal fluid contained 40 cells, mainly polymorphonuclear ones, per c.mm. and Gram-positive diplococci. The neck was moderately stiff and Kernig's sign was positive. Twenty thousand units of penicillin in 10 cc. normal saline were given intrathecally and 100,000 units intramuscularly every three hours. The temperature came down to normal and has remained at that level since then. On 31st December, lumbar puncture was again repeated, the fluid was slightly hazy but tension was normal.

Twenty thousand units of penicillin in 10 cc. of normal saline were given intrathecally in addition to intramuscular penicillin. On 1st January, 1950, the patient was much better, neck became soft but Kernig's sign was slightly positive. He made uninterrupted recovery. Penicillin was given for five days and sulphadiazine for 9 days.

Discussion

The first patient was admitted in deep coma. She had complained of severe constant headache for two days before she fell down and became unconscious within a few hours of the accident. The deep coma may be responsible for the absence of neck rigidity and for negative Kernig's sign.

The second patient was admitted with history of continuous fever and pain around umbilicus for 6 days. On admission cerebrospinal fluid was normal and blood did not show any leucocytosis. Along with that, he never had during the whole course of the disease any neck rigidity or positive Kernig's sign. These facts made one hesitate in making a diagnosis of meningitis though the clinical picture was very suggestive of the disease and second lumbar puncture was not done till the eighth day of his admission in the hospital. It is known that fever with pain around umbilicus is one of the uncommon modes of onset of meningitis in children. Pathological changes in the meninges may not have been sufficient to produce nuchal rigidity and positive Kernig's sign.

The third patient was admitted as a suspected case of malignant malaria. The blood did not show any malarial parasites and polymorphonuclear leucocytosis was present. On the day of admission, which was the fourth day of the disease, the neck was soft, Kernig's sign was negative and cerebrospinal fluid was normal. On the sixth day of the disease the fluid became turbid and contained pus cells and Gram-positive diplococci, the neck then became slightly stiff and Kernig's sign was slightly positive.

Summary

Three cases of pneumococcal meningitis with atypical features have been described.

Though neck rigidity and positive Kernig's sign are characteristic signs of meningitis, they may be absent at the initial stage of the disease and in rare cases throughout the whole course of the illness.

A plea is made for early lumbar puncture and chemical, microscopical and cultural examination of the fluid in suspected cases of meningitis even in the absence of neck rigidity and of positive Kernig's sign. Thereby, valuable time may not be lost in the institution of specific treatment.

My grateful thanks are due to Dr. D. C. Chakraverty, M.B., F.R.C.S. (Edin.), Superintendent of the Medical College Hospitals, Calcutta, for the permission to report these cases.

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RHEUMATOID ARTHRITIS IN A CHILD WITH UNUSUAL MANIFESTATIONS

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In recent times emphasis in rheumatoid arthritis has shifted from the locomotor system and there is growing realization of the extensive nature of the condition. Ellman and Ball (1948) made a suggestion for alteration of the nomenclature from rheumatoid arthritis to rheumatoid disease in conformity with this realization.

Of the non-arthritic manifestations in this disease, periodic pyrexia was noted by Still in his original description. In Schlesinger's (1949) series of twenty cases of rheumatoid arthritis, sixteen suffered from phasic pyrexia but he noted that the periods of pyrexia were never well defined. High pyrexia is a rarity in this disease. As Short (1949) puts it 'Modern authors confine themselves to the statement that the temperature may rise to 102°F. or 103°F.'. Banatyne in 1896 recorded a temperature of 105°F. on one occasion. Only recently Short (1949) mentioned another case where temperature of 105°F. was recorded on two occasions. Rash was noted by Schlesinger (1949) in fifteen of his series. It is more common in the early stages and often disappears with the more chronicity of the disease. The rash is maculopapular and erythematous, widespread in its distribution, and its intensity varies more or less with the temperature.

Clinical features of the following case deserve attention because of the well-defined phasic pyrexia, frequent high intermittent rise of temperature and the persistence of the rash in spite of the disease being present for nearly two years.

The patient, a boy, aged 10 years, came to the out-patient department of the Lake Medical College Hospitals on 13th August, 1949. He gave a history of having several attacks of fever associated with chill and rigor, and pain in many joints for one and a half years. About two months ago fever returned with rash all over the body and swelling of the right ankle joint. The temperature and rash subsided but the joint swelling persisted. Again after a few days temperature with rash returned and more joints became involved—the left ankle and both wrists.

He was pale and emaciated. His temperature was 99°F. Pulse rate was 95 per minute and blood pressure 100/70 Hg. mm. The intercarpal joints of both hands showed definite swelling, tenderness and some limitations of

movement. The tarsal joints of both feet were tender with limitation of movement though there was no evident swelling. The tonsils were enlarged. The skin all over and more specially of the groin was unhealthy and the inguinal glands were enlarged and tender. Examination of all other systems was negative and no nodules elsewhere were found.

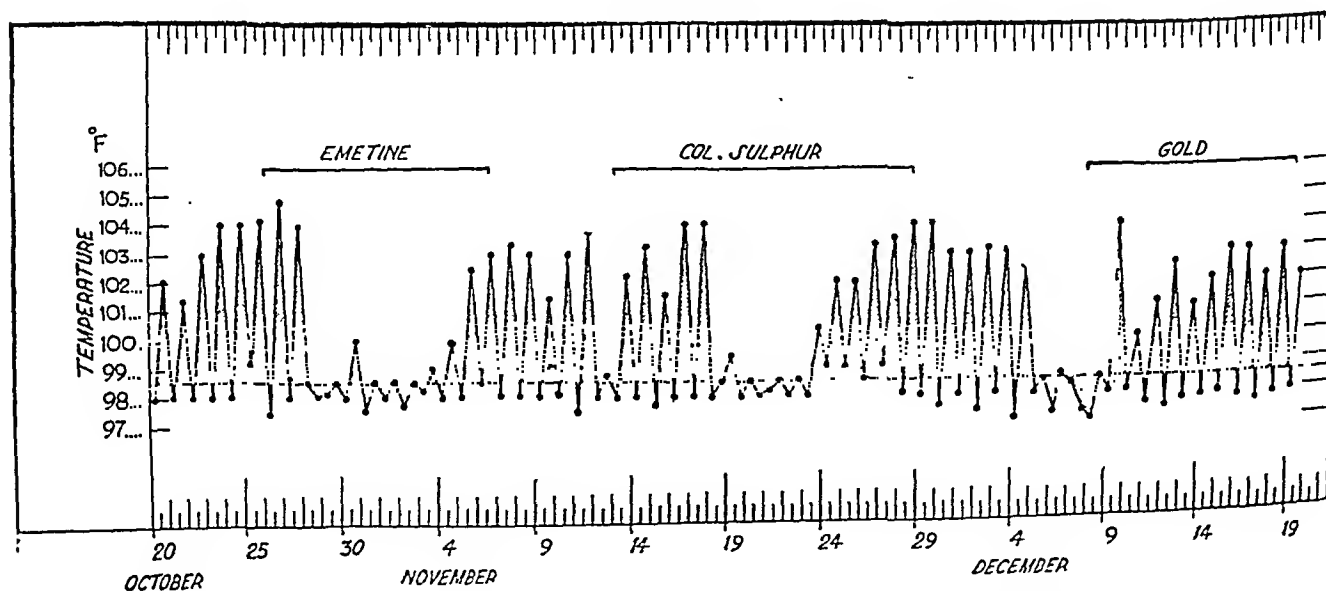
Three days after admission he had a temperature of 102.8°F. which came with a rigor and there was diffuse erythematous, maculopapular rash all over the body including the face. The temperature came down to normal in twelve hours along with disappearance of the rash. This intermittent fever with rash continued for nine days. A blood examination revealed total leucocytes 8,000 (neutrophils 79 per cent, lymphocytes 18 per cent, eosinophils 3 per cent), Hb. 54 per cent and red cells 2,970,000. Blood culture was sterile. No malarial parasites were detected in the peripheral blood smears. Urine culture was sterile. Radiographs of the affected joints showed no evident abnormality. He was put on penicillin empirically. At the end of the pyrexial phase he remained afebrile for five days to be followed by reappearance of intermittent fever and rash. This lasted for a week. During this period one day highest temperature recorded was 104.2°F. All told he got 3 mega units of penicillin parenterally when it was discontinued. After an apyrexial phase of two days he started again on 30th September, 1949, the third pyrexial bout which lasted for twelve days and on one occasion the temperature went up to 104.8°F. Along with high intermittent fever and rash he developed migrating arthralgia and exacerbation of the swellings and tenderness of carpal joints of both hands. Examination of the patient did not reveal any change except that the skin was healthy and no lymphadenopathy could be detected. A blood examination revealed 6,800 total leucocytes, neutrophils 80 per cent, lympho-

cytes 19 per cent, eosinophils 1 per cent, Hb. 44 per cent, red cells 2,370,000. Blood culture was sterile. Aldehyde test and Chopra test were negative. Blood smear for *Spirillum minus* and *Microfilaria bancrofti* proved negative. Serum agglutination test for Brucellosis was negative. Urine culture was sterile. Skiagram of the chest showed no abnormality. During this pyrexial phase an antihistamine therapy was instituted, both orally and parenterally. After an apyrexial period of two days the same bout of fever and rash returned and continued for ten days. The temperature during this attack reached 104°F. on four occasions while once it touched 105°F. Antihistamine drug was discontinued as it failed to prevent or modify the appearance of rash. He was put on emetine empirically on 28th October, 1949, which coincided with the beginning of another apyrexial phase. This time he remained practically free from fever for one week (the longest apyrexial period) at the end of which commenced the fifth pyrexial bout lasting for twelve days and having 104°F. temperature on two occasions. There was swelling of distal interphalangeal joints of index finger of both hands. He was put on colloidal sulphur. After an apyrexial period of five days he developed the sixth bout of fever. This lasted for eleven days. He complained of migrating arthralgia. Gold therapy was instituted during this period and was continued through the following apyrexial phase of three days. On 19th December, 1949, he started the seventh similar pyrexial symptom complex: High intermittent fever coming on with chill, profuse erythematous rash and arthritis.

Therapy and progress

He was put on sodium salicylate for three weeks without benefit. Treatment with ascabiol (a benzyl benzoate product) improved his skin and caused disappearance of inguinal lymphadenopathy (for other therapeutic trials see charts 1 and 2). His weight on admission was 41 lb.

CHART 1



and he gained 4 lb. in seven weeks. Thereafter he progressively lost weight. Radiographically the carpal bones showed no decalcification. The movement of the joints—metatarsal joints of both feet—are limited. Swelling, pain and tenderness of carpal joints of both hands have remained unaltered. The distal interphalangeal joints of index finger of both hands are still swollen and tender with marked limitation of movement. The fever and rash continue to appear periodically and unabated.

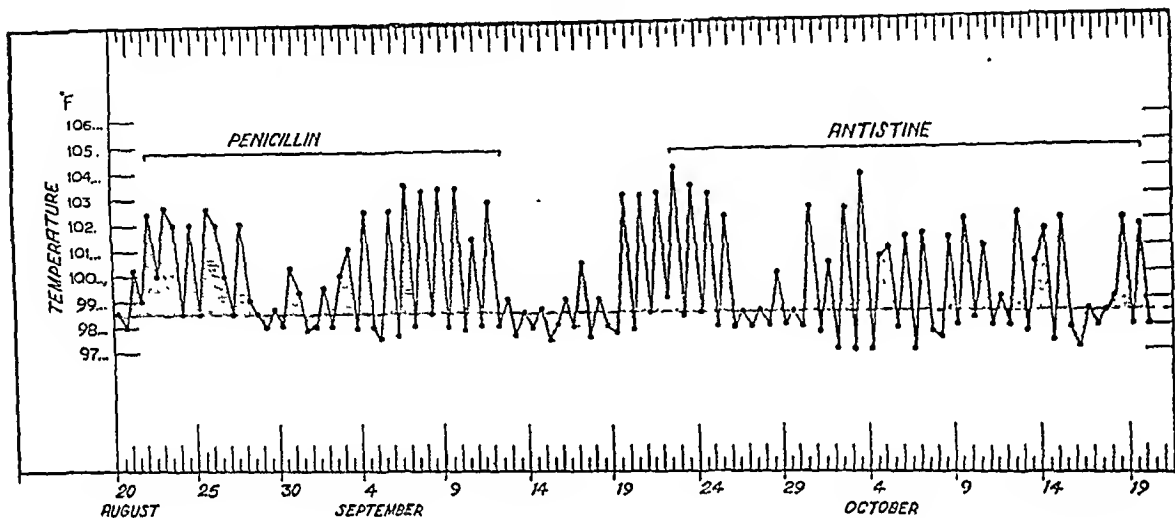
THE INCIDENCE AND DISTRIBUTION OF MURINE TYPHUS AMONGST BOMBAY RATS

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ENDEMIC typhus is undoubtedly the most widespread of rickettsial group of infections. Bombay, an active tropical port, with its popula-

CHART 2



Summary

A case of rheumatoid arthritis has been described in which well-defined phasic pyrexia was characteristically observed. The pyrexia simulated pyogenic infection because of its high intermittent nature and being associated with chill and rigor. On several occasions a temperature of 104°F. was recorded while on one occasion it went up to 105°F. The diffuse erythematous maculopapular rash was another prominent feature in this case. Adenopathy which is often mentioned in rheumatoid arthritis in childhood was conspicuously absent.

My thanks are due to Captain K. L. Sen, the Superintendent cum Principal, Lake Medical College Hospitals, Calcutta, for his kind permission to report this case.

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tion of rats and fleas, and congested living conditions, fulfils all known requisites for propagation of this type of rickettsial infection. While the isolation of strains from typhus cases reported by the author (1947a) and the epidemiological studies by Savor, Valia and Soman (1948) have appropriately suggested the occurrence of typhus of murine origin and incriminated rat as the principal reservoir, very few observations have been made on the incidence and distribution of murine typhus in Bombay rats beyond some casual data presented by Stoker (1948). The use of complement fixation test is now widely adopted in the diagnosis of various virus and rickettsial diseases and affords a reliable and economic means of performing rodent surveys (Brigham and Bengston, 1945). A preliminary comparative study by the writer (1947b) of Weil-Felix, complement fixation and rickettsial agglutination tests revealed that the complement fixation test was much more specific and reliable than the other two tests. With limited supplies of specific rickettsial antigens, it became possible to work out the incidence of murine typhus in Bombay rats and study its distribution in different species. These antigens were obtained through the courtesy of overseas virus and rickettsial workers. The results of such an investigation carried out for two years form the subject-matter of this paper.

Materials and methods

Approximately 2,000 rats trapped all over the city of Bombay were sent to Haffkine Institute every day for evidence of plague infection. On identification, they belonged to the following species, *Rattus rattus* 19.6 per cent, *R. norvegicus* 23.7 per cent, *Gunomys kok* 49 per cent, *Suncus coeruleus* 3.5 per cent (shrew), *Bandicota malabarica* 1.7 per cent, *Mus dubius* 2.5 per cent. The first three of these comprised nearly 92 per cent of the trapped number, which were chiefly used for this investigation. A small number of the species *Suncus coeruleus* was also used for examination. After identification, the rats were lightly anaesthetized to collect any ectoparasites such as fleas, ticks and mites. They were then bled by cardiac puncture and clear sera were collected. When not immediately used, the sera were merthiolated and preserved in the

treated by the method described by Taran (1946) before the complement fixation was carried out. Many such sera could be tested in this way, which otherwise would have been discarded.

Results

During the period under investigation, 739 rodents were examined; these included 323 *Rattus rattus-rufescens* (house rat), 193 *Rattus norvegicus* (sewer rat), and 208 *Gunomys kok* (field rat). Only 15 shrews of the species *Suncus coeruleus* were available for examination. The other two species, namely *Bandicota malabarica* (field rat) and *Mus dubius* (mouse), were not obtainable for examination. The results of the complement fixation tests with murine antigen on 739 rodent sera and 50 laboratory-bred white rats are summarized in table I:—

TABLE I

Species of rat	Total examined	Number positive as per titre, C.F.				Total positive	Percentage positive
		5	10	20	40		
<i>R. rattus</i>	323	48	7	4	3	62	19.2
<i>R. norvegicus</i>	193	25	12	20	27	84	45.0
<i>Gunomys</i>	208	6	4	3	0	13	6.2
<i>Suncus</i> (shrew)	15	0	0	0	0	0	0.0
	739	79	23	27	30	159	24.22
Laboratory-bred white rats ..	50	0	0	0	0	0	0.0

refrigerator. Whenever isolation of strains from rats was desired, pooled brains of 3 to 8 rats of the same species were ground together with sterile glass powder and a saline suspension obtained. The supernatant fluid was used to inoculate male guinea-pigs intraperitoneally. The few fleas that were collected were mostly *X. cheopis* and were not used for isolation of strains. But trombiculid mites were collected in good numbers, half of which was stored for identification and the remaining half in a pool of 60 to 80 was used for isolation of strains.

For complement fixation test, Bengston's (1944) technique was followed with slight modification. The test was performed using murine antigen, three full units of the complement in 0.25 cc., 3 per cent sensitized sheep cells, utilizing 3 units of amboceptor and the serum dilution of 0.25 cc., starting at a dilution of 1 : 5. Fixation was carried out at 37°C. for one hour and the reaction with the hæmolytic system was carried out at 37°C. for half an hour. In all sera, which showed fixation at a dilution of 1 : 5, the test was repeated in higher dilution up to 1 : 40. Whenever some rat sera were found to be anticomplementary, they were

The titres observed were generally low, nearly 50 per cent being 1 : 5. Titres above 1 : 40 were not routinely carried out for want of stock of sufficient antigen, but some of these sera when tested further, showed titres as high as 1 : 320. That 27 *Norvegicus* rat sera should fix the complement in as high titres as 1 : 40 was an interesting finding, the significance of which is discussed later.

Weil-Felix test carried out with 26 sera positive by complement fixation test showed that agglutination with proteus strains occurred in very low titres not exceeding 1 : 40 and they could not be taken as diagnostic or indicative of any past or recent infection. There were 11 sera out of 26 which agglutinated proteus OXK suspension in low titres of 5 and 10 and 4 sera which agglutinated proteus OX2 suspension in the same way. The significance of these findings is discussed later.

In all, 34 attempts were made to isolate strains from 119 rodents by inoculating guinea-pigs intraperitoneally with pooled brain suspension. The inoculation was done irrespective of the results of complement fixation tests. Two strains could be isolated from two species of

rats, *Rattus rattus* and *Rattus norvegicus*. In the presence of pyrexia but without a serotal reaction, the guinea-pigs were allowed to be convalescent when their sera were collected for demonstration of complement-fixing antibodies. Two more pools of *Rattus norvegicus* were thus indirectly shown to be infective, although no rickettsia could be actually demonstrated. Thus three pools of *Norvegicus* rats and one pool of *Rattus rattus* were shown to be infective by the animal experiments. In five attempts to isolate strains from *Gunomys* rats, the guinea-pigs showed no febrile reaction when observed for a period of 21 days and showed no complement-fixing antibodies in their sera. Similarly, in 9 attempts made to isolate strains from shrews, only 4 guinea-pigs showed erratic type of fever. Thus no rickettsial strains could be isolated from either *Gunomys* or *Suncus*. Table II illustrates some of the representative results :—

absence of another male guinea-pig. These rats after 45 days were again passaged into a male guinea-pig which developed pyrexia and serotal reaction 11 days after the inoculation. Smears prepared from the tunica exudate and stained with Giemsa showed abundant intracytoplasmic inclusions indistinguishable from *R. mooseri*. Cross immunity test using this strain and the standard 'Wilmington strain' indicated complete reciprocal protection to inoculated guinea-pigs, with no febrile or serotal reaction. Further passages were obtained in guinea-pigs and white rats; the rat sera when tested after a period of 510 days still showed the presence of complement-fixing antibody in a titre of 1 : 40 and the brain still proved to be infective on further passage.

Strain *R. n.*

This strain was isolated from three *R. norvegicus* in June 1947. Two out of three

TABLE II

Number of pool	Month of inoculation	Number of rats in a pool	C.F. test on rat sera	RESULTS OF GUINEA-PIG INOCULATION		
				Fever	Serotal reaction	C.F. test
1	May 1946	4 (<i>R. rattus</i>)	+	+	<i>R. mooseri</i>	..
2	May 1946	5 (<i>R. rattus</i>)	..	+	—	..
3	May 1946	2 (<i>R. rattus</i>)	+	+	—	—
4	July 1947	3 (<i>R. rattus</i>)	+	+	<i>R. mooseri</i>	+
5	July 1947	4 (<i>R. norvegicus</i>)	—	+	—	+
6	July 1947	3 (<i>R. norvegicus</i>)	+	+	—	—
7	July 1947	2 (<i>R. norvegicus</i>)	+	+	—	+
8	August 1947	2 (<i>R. norvegicus</i>)	..	+	—	—

The relation of a positive and negative complement fixation test to the isolation of virus is discussed later.

In the meanwhile, it would be interesting to note and compare the results of pool numbers 5 and 7, in which virus could be isolated irrespective of the positive or negative test; while pool number 6 showed that virus could not be isolated in spite of a positive complement fixation test.

Strain *R. r.*

This strain was isolated from four rats (*Rattus rattus*) captured between 20th May, 1946 and 22nd May, 1946. Serum of one of these rats showed a positive complement fixation titre of 1 : 40 as was reported by Captain Stoker of the Field Typhus Research Unit Laboratory, Poona (personal communication). An intraperitoneal inoculation of a male guinea-pig with a pooled-brain suspension of four *Rattus rattus* elicited a febrile response after an incubation period of 6 days without any serotal reaction. On the 3rd day of fever, the guinea-pig was passaged into 2 white rats, in the

rats showed a positive complement fixation titre of 1 : 10 and 1 : 40. A similar technique was adopted to isolate the strain and the guinea-pig reacted with high temperature and the serotal reaction after 8 days of inoculation. *R. mooseri* were easily demonstrated in the Giemsa-stained smears from the tunica exudate. Further passages were obtained in guinea-pigs and white rats. Guinea-pig sera tested on the 8th or 9th day after inoculation were found to be negative by complement fixation test, but those tested after 30 and 78 days were found positive with a titre of 1 : 80 and 1 : 40 respectively. Passage rat sera also tested similarly after 48 and 152 days showed positive complement fixation test with a titre of 1 : 40 and 1 : 20 respectively. Although no cross immunity experiments were done with this strain, the results of complement fixation test using murine antigen proved beyond doubt that the strain was of murine origin.

Survival of murine virus in laboratory-bred white rats

This experiment was planned to throw some light on the epidemiology of typhus infection in

Bombay. Two murine strains, one from Bombay rats and one from a typhus case, were used for inoculation of two laboratory-bred white rats separately. The rats were observed for a period of 510 and 522 days respectively, at the end of which their brains were passaged into two male guinea-pigs separately. Their heart bloods were collected at the same time and complement fixation tests were carried out with their sera and the sera of experimental guinea-pigs. The results are tabulated below:—

		Period of observation	C.F. test on rat sera	GUINEA-PIG INOCULATION		
				Fever	Scrotal reaction	C.F.
Rat no. 1	..	510 days	+ (40)	+	—	+ (20)
Rat no. 2	..	522 days	+ (20)	+	+	+ (5)

Ectoparasites

Fleas collected from different species of rats were so few that they were not used for isolation of strains, but only for identification. No ticks could be found on the rats examined. Trombiculid mites, however, were collected in large number, the total being 2,628. 1,558 were picked up from *Gunomys*, 990 from *R. norvegicus*, and 50 from *R. rattus*. None of the shrews thus examined showed any mite infestation. On their animal hosts, larval mites were found attached in closely packed orange-red to whitish colonies, numbering up to 200 or more individuals in each. Colonies were usually situated in the conchæ of the ears, on the ear margins and rarely in the regions of genitalia. Usually half the number collected was kept for identification and the other half used for isolation of strains. So far only two species, namely *T. muris* (*indica*) and *T. paltai*, have been identified. Another lot was sent to Dr. Muesebeck, Chief of the Bureau of Insect Identification, Department of Agriculture, Washington, D.C. According to the report, they belonged to species *Euschongastia indica* (Hirst). As previously pointed out, no mite strains could be isolated in spite of six attempts.

Discussion

The object of this investigation was to study the incidence and distribution of murine typhus amongst Bombay rodents. Complement fixation test using murine antigen showed that 159 out of 739 rodents, i.e. 24.22 per cent, had suffered from previous murine infection. Further, rickettsial infection in those rodents was confirmed by the isolation of two strains. The cross immunity test, the source and the behaviour in experimental animals and complement fixation test proved that they were strains of murine typhus. The distribution of antibodies to murine virus in different species of rats and

shrews examined as referred to in table I clearly showed that *R. norvegicus*, the drain rat, was the most commonly affected, the next being *R. rattus*. The species *Gunomys kok* showed the least incidence and the very small number of shrews examined were all negative with the serological tests. The only available and comparable data in India is that of Stoker (1948), who found 9.3 per cent as the overall incidence of murine typhus in 75 Bombay rats. This low figure could be easily accounted for, since

R. norvegicus examined in his series were only 9. On the other hand, his incidence figures in *R. rattus* and *Gunomys* were in close agreement with those obtained in this investigation. He also found sera from 12 voles from Poona, negative by complement fixation test, which was also seen in this investigation. His general incidence was found low because *R. norvegicus* which showed very high incidence was included in his series in negligible numbers. Although no strain from *Gunomys* was isolated in Bombay, he had done so from the species in Poona. Similarly, Savor, Vahia and Soman (1948) had also previously isolated a strain from rats, trapped in the house where a typhus case had occurred.

A study by Brigham and Bengston (1945) of complement fixation test as related to the isolation of murine virus showed that the correlation was poor in the case of naturally infected wild rats. Positive serological findings apparently persisted much longer than transmissible virus and no titre range could be established indicating present infections. A reference to the table case nos. 4, 6, and 7 has shown that while the C.F. test was positive in two pools, only from one pool could the virus be isolated. It follows, therefore, that although 24.22 per cent of rats on the whole showed positive C.F. test, it does not necessarily connote that this proportion was actually infective at the time. The test probably remains positive for the rest of the animal's life and the low titre met with special reference to *R. rattus* and *Gunomys* sera, similar to those obtained by Woodward, Philip and Loranger (1946), suggest that most of the infections were not recent. Although higher titres in connection with sera of *R. norvegicus* were not tested, it is probable that species predominantly showed the recent active infection.

The murine virus is known to survive in laboratory-bred white rats quite for a long time.

Philip and Parker (1938) have reported 370 days as the longest survival period. In this investigation it was found that the virus could be isolated from such rats inoculated as long as 510 and 522 days. This observation naturally possesses a significant value in the epidemiology of this disease. It is highly probable that wild rats once infected in nature maintain and propagate the infection from year to year and thus act as efficient reservoir hosts. In this way, *R. norvegicus* appears to be the species chiefly responsible for the carry-over of virus from one season to the other. This is further supported by the high titres obtained by C.F. tests. Other species were not investigated in sufficient numbers or not investigated at all, such as *Bandicota malabarica* and *Mus dubius*, because these were obtained in very small numbers, rarely coming in contact or invading human habitations.

Summary

1. The incidence and distribution of murine typhus in field and domesticated rodents in Bombay were assessed by complement fixation test.

2. Evidence of previous infection was obtained in 24.22 per cent of 739 rats examined on the whole. The distribution among different species was calculated: *R. norvegicus* showed an incidence of 45 per cent, *Rattus rattus* 19.2 per cent and *Gunomys kok* only 6.2 per cent. The small number of shrews examined showed no evidence of previous infection.

3. Rickettsial infection amongst the rodents in Bombay was further confirmed by the isolation of two strains. Cross immunity and complement fixation tests conclusively proved that the strains were of murine origin.

4. The longest survival period of murine virus as obtained in an experimentally infected laboratory-bred rat was 522 days, proving the efficacy of the rodent reservoir in the maintenance and propagation of virus in nature from year to year.

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STREPTOMYCIN IN SYPHILIS

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 and ;

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In earlier days of penicillin it was believed that this antibiotic had little effect on *Trep. pallidum*. But after some years of experience and observations it has been found to have almost superseded arsenicals in the treatment of syphilis. General opinion at present is that streptomycin is of very little use in this disease. Willcox in 1948 reported that 0.6 gm. of streptomycin in one dose had no effect on *Trep. pallidum* obtained from the sore. Taggart *et al.* in 1948 reported similar results when trying streptomycin *in vitro*. The idea was to find out a drug for the treatment of acute gonorrhoea, which will not mask the serological or microscopic tests for syphilis when concomitant infection may be present.

Here we are reporting a few cases of early secondary syphilis with rash and joint pains, Kahn and W.R. strongly positive, treated with streptomycin. Unfortunately, we like the other workers in our country found it difficult to follow up these cases for any length of time. And only four cases out of ten could be followed for a period of three months. All the selected cases were 'virgin' cases, in the sense that they had never suffered from any venereal disease before nor received any kind of treatment either with arsenic, bismuth or penicillin during this illness. S.T.S. were done before starting the treatment and weekly afterwards on completion of the treatment.

Report of serological tests

Num- ber	Name	Age, years	Sex	Before treatment	AFTER TREATMENT												
					1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	8th week	9th week	10th week	11th week	12th week	18th week
1	R. J.	22	M.	W.R.	+	+	+	-ve	-ve
2	R. A.	20	M.	K.T.	+	+	+	-ve	+	-ve
3	B. P. J.	33	M.	K.T.	+	+	+	+
4	B. M. B.	22	M.	W.R.	+	+	+	+	+	-ve
5	D. T.	20	M.	K.T.	+	+	+	+	+	+
6	A. G. N.	22	M.	W.R.	-ve	-ve	-ve	-ve	-ve	-ve
7	P. S.	25	M.	K.T.	+	+	+	-ve	-ve
8	N. G.	22	M.	W.R.	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
9	R. M. K.	24	M.	K.T.	+	+	+	+	+	+	+	+	+	+	+	+	..
10	P. S. N.	22	M.	W.R.	+	+	+	+	+	+	+	+	+	+	+	+	..
11	G. S. C.	28	M.	K.T.	+	+	+	+	+	+	+	+	+	+	+	+	..
12	K. T. M.	20	M.	W.R.	+	+	+	+	+	+	+	+	+	+	+	+	..

* Case 7.—C.S.F. was -ve for Kahn and W.R. and no abnormality was detected.

Dosages.—9.5 gm. of streptomycin in 15 divided doses over 7½ days' period. This dose was approximately calculated on the basis of penicillin and streptomycin ratio for cure of acute gonorrhoea.

Toxic reactions.—Only one case, no. 5, developed allergic reaction in the form of itching and macular eruptions which promptly reacted to antisthen tablets (Ciha) by mouth. No other reactions were noted.

Observations

1. Rash took about two weeks to disappear after the treatment, though joint pains subsided after 5 to 6 weeks completely.

2. W.R. became completely negative in majority of cases in about 4 weeks' time and Kahn was doubtful or negative at the end of the 7th or 8th week. From this we find that Kahn test took longer time to become negative than W.R.! Does this suggest that more reliance may be kept on Kahn test for serological cure of syphilis? May be, that the biological cure is attained very soon after the treatment but only the reagin takes longer time to disappear.

3. In view of our findings we feel that streptomycin like penicillin should not be the drug of choice for acute gonococcal infection if the concomitant infection is expected, unless the patient is able to be followed up for S.T.S. for at least 3 to 6 months.

4. It will be interesting to observe if the period of infectivity to the other partner is reduced by this drug and the minimum dose necessary to obtain this result. Perhaps this drug may be able to reduce the incidence of neurological complications and congenital infections in syphilis.

5. Our findings lead us to believe that for prophylactic treatment streptomycin should replace penicillin. Penicillin, as we know, does not abort or cure all the venereal infections, e.g. chancroid, granuloma inguinale, etc. But streptomycin acts on all the venereal diseases and thus may prove a really more useful drug with arsenic and bismuth for abortive treatment.

We thank the Civil Surgeon, Sassoon Hospitals, for allowing us to report these cases and the Principal and the staff of the Pathology Department of B. J. Medical College for helping us in our investigation. Squibb & Co. were good enough to supply the drug free for these trials.

A Mirror of Hospital Practice

A CASE OF SCIATICA DUE TO MALARIA

By AMRIT LAL WAHI, M.B., B.S.

Deeg (Dist. Bharatpur)

N. S., a Hindu male, aged 50 years, reported to me with the complaint of pain in the back of

right leg, from the hip to the foot, of six months' duration. The pain was of a burning nature and spread from the right hip to the external aspect of the toes of the right foot. The pain was constant but was worse at night.

Past history.—The patient was an agriculturist by profession and had been lifting heavy weight during the performance of his duties. On one occasion he strained the muscles of his anterior abdominal wall while lifting weight and the pain persisted for about a fortnight. No history of pain in back prior to this complaint. He gave history of irregular fever lasting for over a month prior to his present complaint.

C. O. E.: (1) *Local.*—The patient was not able to stand erect. He kept his right lower limb flexed at the hip and knee joints and extended at the ankle and stood on his toes. He walked in the same position and limped on walking. Kernig's sign was positive in the right lower limb. The course of the sciatic nerve was tender on pressure. Measurements of the limb were normal. Sensory and motor functions of the limb were normal. Tendon jerks were normal. Nothing abnormal was detected on examination of the patient per rectum.

(2) *General.*—Nothing abnormal was detected except that the spleen was palpable and hard.

Treatment.—As the patient gave history of irregular fever before the onset of the present complaint and had a palpable spleen, I thought it advisable to carry out the antimalarial treatment before proceeding with anything else. I put the patient on the following mixture:

R

Quinine sulph.	..	7 grs.
Acid sulph. dil.	..	7 m.
Aq. ad	..	1 5.

Sig:—one t.i.d.

The next morning the patient felt a lot of relief and was able to stand erect though the course of the sciatic nerve was still tender on pressure. The treatment was continued with the same mixture for one week, at the end of which the patient felt absolutely fit and all the signs of the disease had disappeared.

Comment.—Barnes Surt recognizes three types of sciatica: (1) Root sciatica, (2) Trunk sciatica and (3) Referred sciatica, and believes that the aetiology of the disease is different in each case. But in the past ten years the importance of a retro-pulsed intervertebral disk as a cause of persistent sciatica has been stressed by many observers to such an extent that other causes or possible causes have been overlooked. So it is suggested that in a tropical country like ours malaria as a cause of sciatica should not be overlooked and should be excluded in every case before proceeding with any big surgical operations such as laminectomy, etc.

A CASE OF INTESTINAL INFESTATION WITH *HYMENOLEPIS DIMINUTA* IN MAN

By A. S. PARANDE, L.M.P., D.T.M.

Nagpur

INTESTINAL infestation with *Hymenolepis diminuta* is not common. In man not more than twenty cases have been reported in India. Its true definitive host is rat, and infestation amongst them is common in this place. In view of the rarity of this condition, the following case is being reported.

Case report

S. D., a young girl, was having pain in the right iliac fossa, with short periods of evening rise of temperature, off and on for the last four years. No history of diarrhoea or dysentery was given nor was there any loss of weight. She was having flatulence of upper abdomen.

Dr. Mrs. P. Raj, W. M. S., Daga Hospital, advised her to get her faeces examined. Examination revealed ova of *Hymenolepis diminuta* (figures 1 and 2, plate XL).

Egg is distinctly yellow in colour.

Outer shell of embryophore is thickened and slightly mammilated.

Hooklets in hexacanth oncosphere are arranged in fan-shape manner.

(Four repeated examinations showed the eggs in each specimen.)

Hymenolepis nana infection in man is relatively common; from the ova of this tapeworm, those of *H. diminuta* are distinguished by the distinct yellow colour, thicker embryophore and fan-shape arrangement of hooklets. The former does not require an intermediate host, whilst in the case of the latter, an arthropod, e.g. rat flea, acts as an intermediate host, in which cysticercus stage develops. Man gets infected by accidental ingestion of infected rat flea infesting prepared cereal foods.

[The eggs of *Hymenolepis diminuta* are bigger than those of *H. nana* and have no filaments in the space between the outer and inner envelopes of the egg.

The infection is due to accidental ingestion of either the infected ectoparasites of the murine host or the infected insects, e.g. meal moths or meal worms living in cereals used for cold cereal breakfast foods—N. V. B.]

AN UNUSUAL CASE OF LYMPHOCELE OF THE SCROTUM

By B. P. TRIBEDI

Professor of Pathology and Bacteriology, Medical College, Calcutta, and Bacteriologist to the Government of West Bengal

RECURRENT filarial attacks produce various changes in the scrotum and conditions such as hydrocele, chylocele and lymph scrotum are well known. In the scrotal sac besides the

various types of fluids, inflammatory cells, red blood cells and filaria sometimes in a dead and calcified condition have been demonstrated. In the present case, in the contents of the scrotal sac the finding was rather rare. So it has been thought worth while to report this case.

B. W., aged 30, male, was admitted into the hospital for the cure of the bilateral hydrocele. The swelling of the scrotum started on the right side about ten years back and went on gradually increasing in size. A year later the left side was also noticed to get bigger. On examination the right side was found to be the size of a no. 2 football and the left one was the size of an orange. On the right side the cord was found to be free and trans-illumination was negative. The whole of the right side was shelled out after an incision. (Tapping had been done when about 4 oz. of straw-coloured somewhat gelatinous fluid had drained out.) On opening the sac, a cauliflower-like mass was seen to occupy practically the whole of the sac. The right testis could not be spotted and the whole mass was thought to be new growth from the right testis. The sac with this mass was removed. The patient's wound healed up, and he left the hospital. The specimen received in formalin preservative was examined and it was found to consist of numerous spherical bodies within the scrotal sac. They did not consist of one mass, but could be easily separated from one another. There was no organic connection between them but they were stuck together as if with glue. The size was that of a pea; but a few were slightly bigger and some were smaller. These pea-like bodies were found not to be firmly attached to the inner wall of the sac but were loosely stuck with a sticky substance. Their surface was uneven and consisted of small granules (see figure, plate XLI). This external appearance was uniform in nature, one was the exact replica of another. The consistency was soft and with slight pressure these could be reduced into a homogenous amorphous dull grey coloured granules. There was no fluid inside. Histological examination showed only a structureless homogenous eosin-stained material without any cellular element. Staining for fat failed to reveal any fatty element.

Comments.—It appears that due to obstruction there was collection of lymph inside the scrotal sac from which these granular bodies were formed. Chemical analysis was not possible because of the formalin fixed specimen. The scrotal sac could not be properly explored to determine the position of the testis or for the abnormalities in the lymphatic because of the possibility of scattering of the spherical bodies and thereby spoiling the specimen. The uniform nature of the physical appearance of all these numerous bodies strongly suggests that the accumulated lymph condensed and granular bodies separated out of it.



Fig. 1.—Case 1. Coloured diagram of the specimen. Note the pale yellowish nodular areas of different sizes.



Fig. 10b.—Case 3. Coloured diagram of the specimen showing the nature of the numerous cysts in detail.



Fig. 6.—Case 2. Coloured diagram of the sagittal section of the tumour showing different coloured areas in the tumour mass.

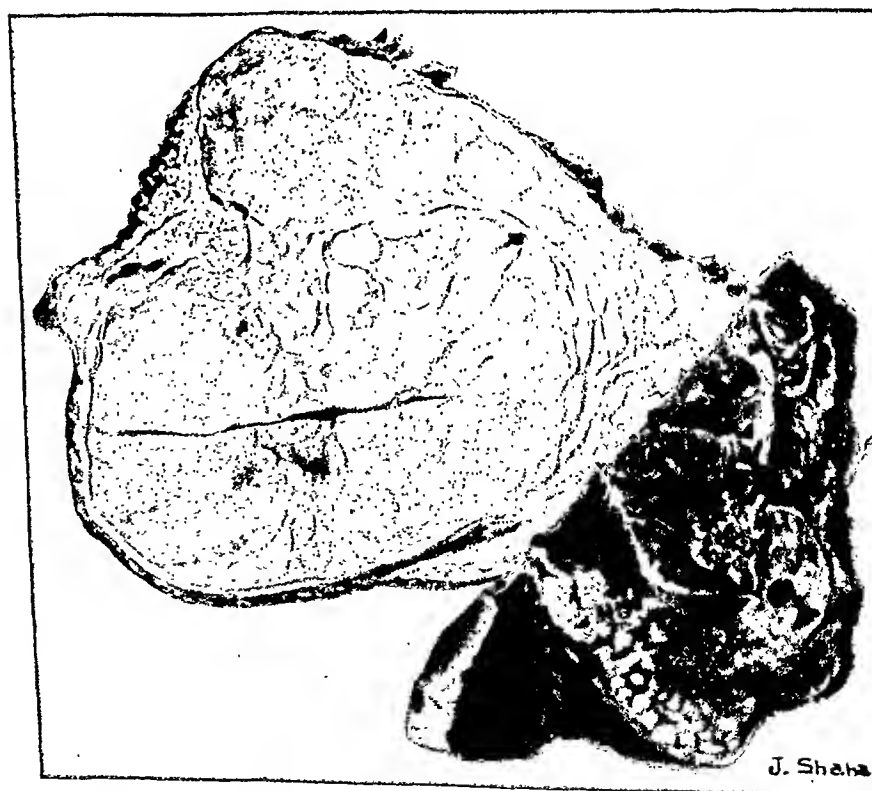


Fig. 15.—Case 4. Coloured diagram of the tumour showing the appearance of the tumour substance.

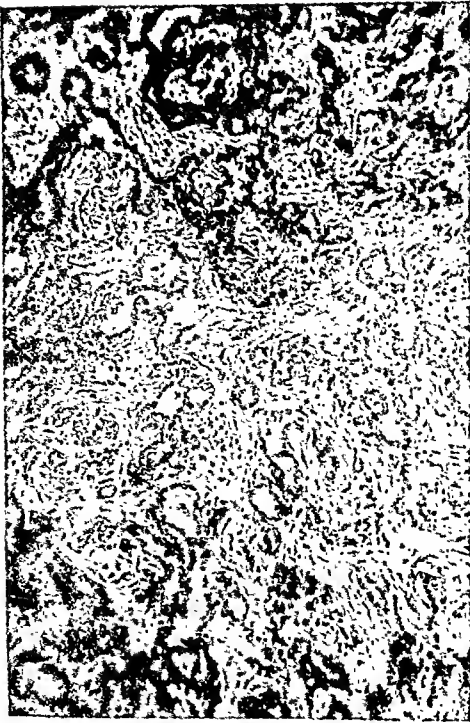


Fig. 2.—Low power photomicrograph from a section made from the smaller nodules. Note the empty tubular spaces lined with cells, some of which show proliferative changes.



Fig. 3.—High power photomicrograph of a section made from one of the bigger nodules, showing compact cellular pattern with mitosis.

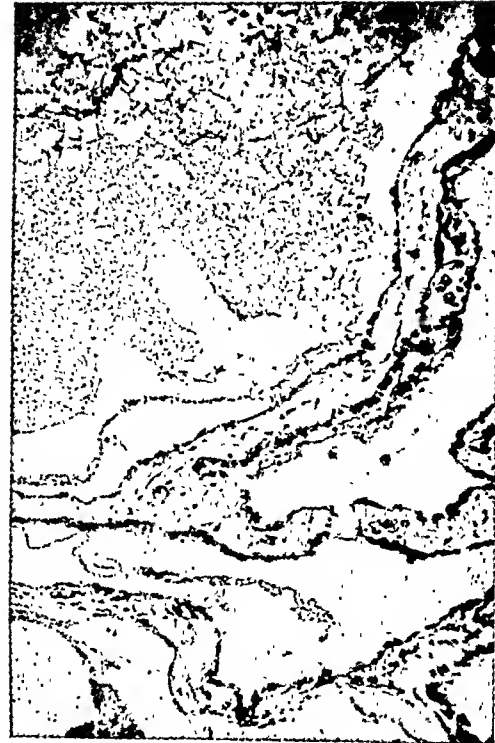


Fig. 4.—High power photomicrograph from one of the bigger cysts showing the structure of the cyst wall and the structure contents of the cyst.



Fig. 5.—Case 2. Skiagram of the tumour showing the thin bony lines in place of the usual bone.

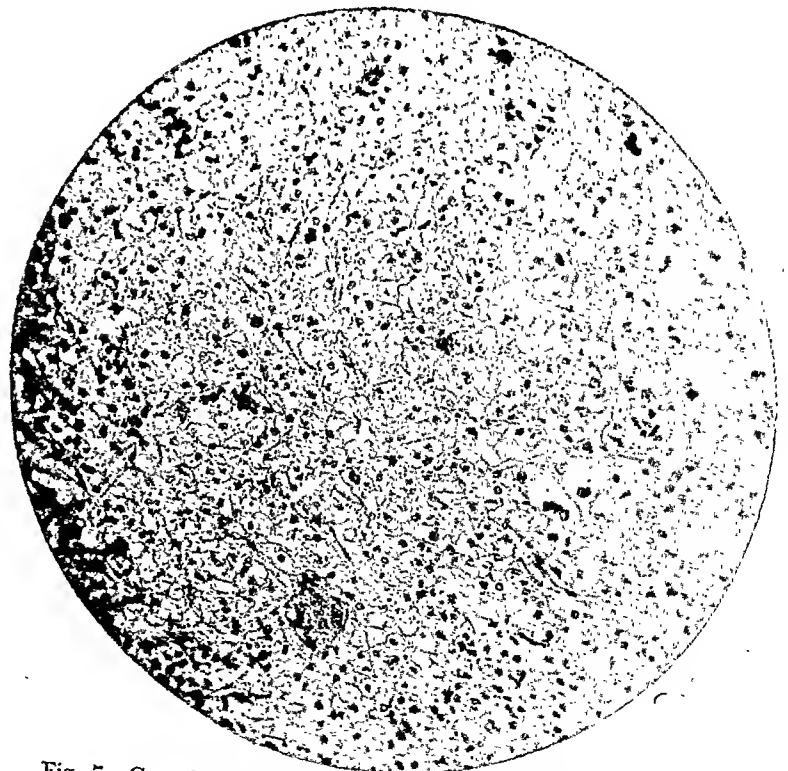


Fig. 7.—Case 2. High power photomicrograph of section showing the appearance of the tumour in the pale areas.

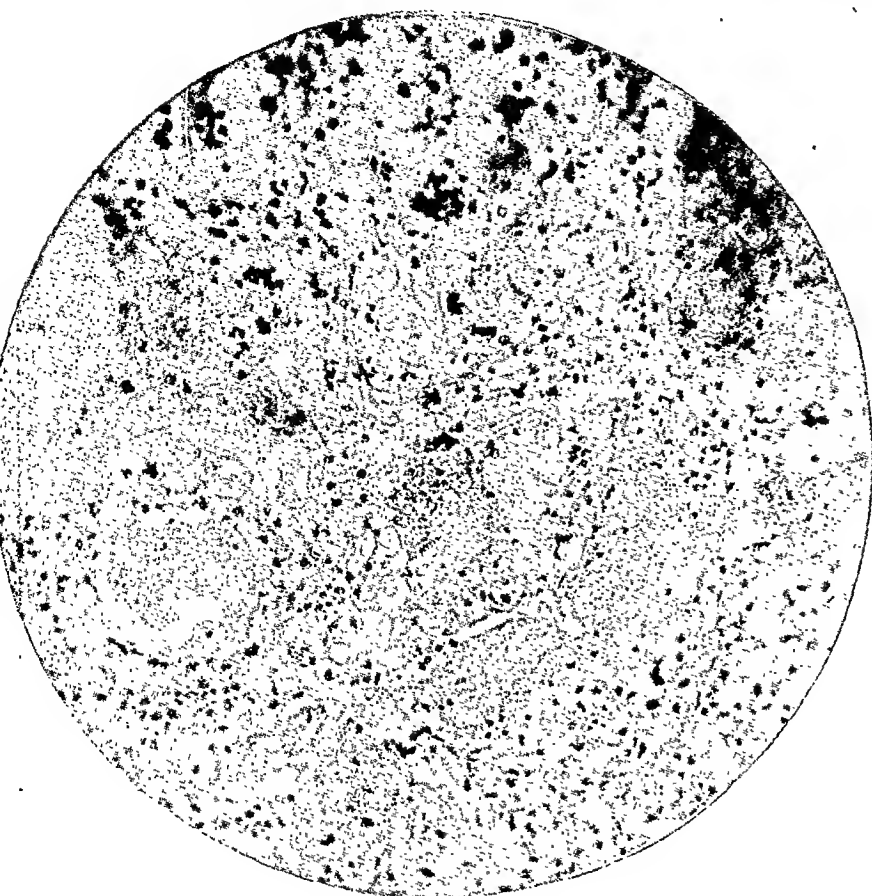


Fig. 8.—Case 2. High power photomicrograph showing large irregular spaces containing blood but without any living endothelium.

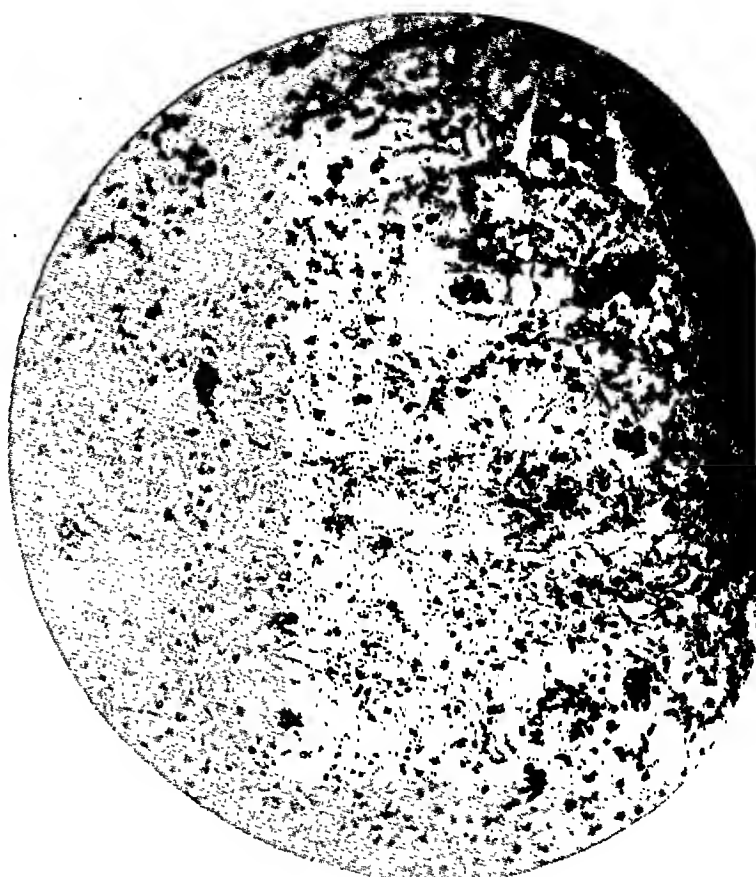


Fig. 9.—Case 2. High power photomicrograph showing areas where there was absence of large blood spaces but irregular cluster-like collection of cells was the dominant feature.



Fig. 10a.—Case 3. Photomicrograph of the specimen showing cysts (mottled).

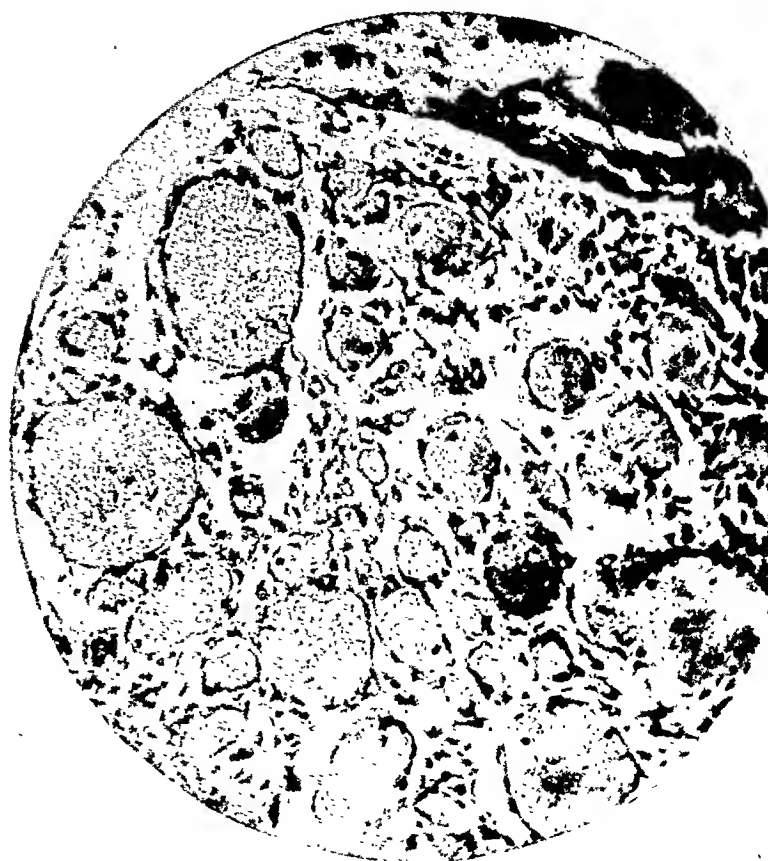


Fig. 11.—Case 3. Photomicrograph of the section from a cystic area. Note the pronounced angiomatous condition.

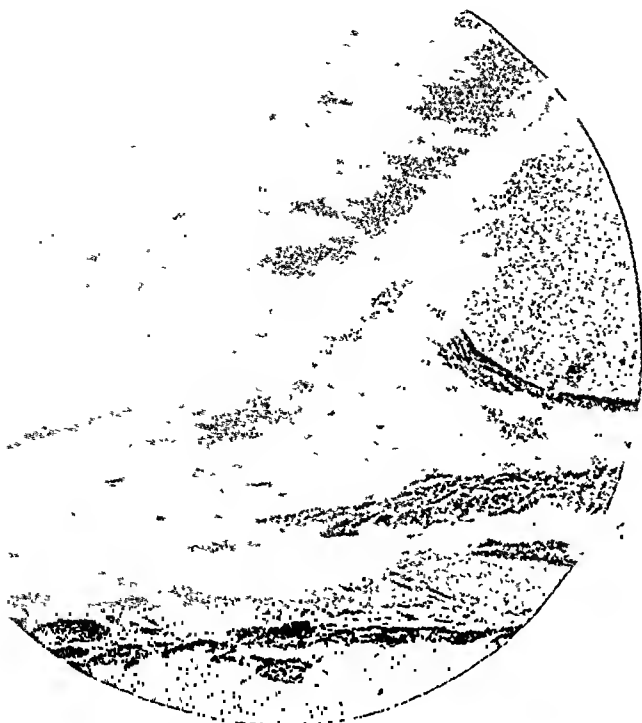


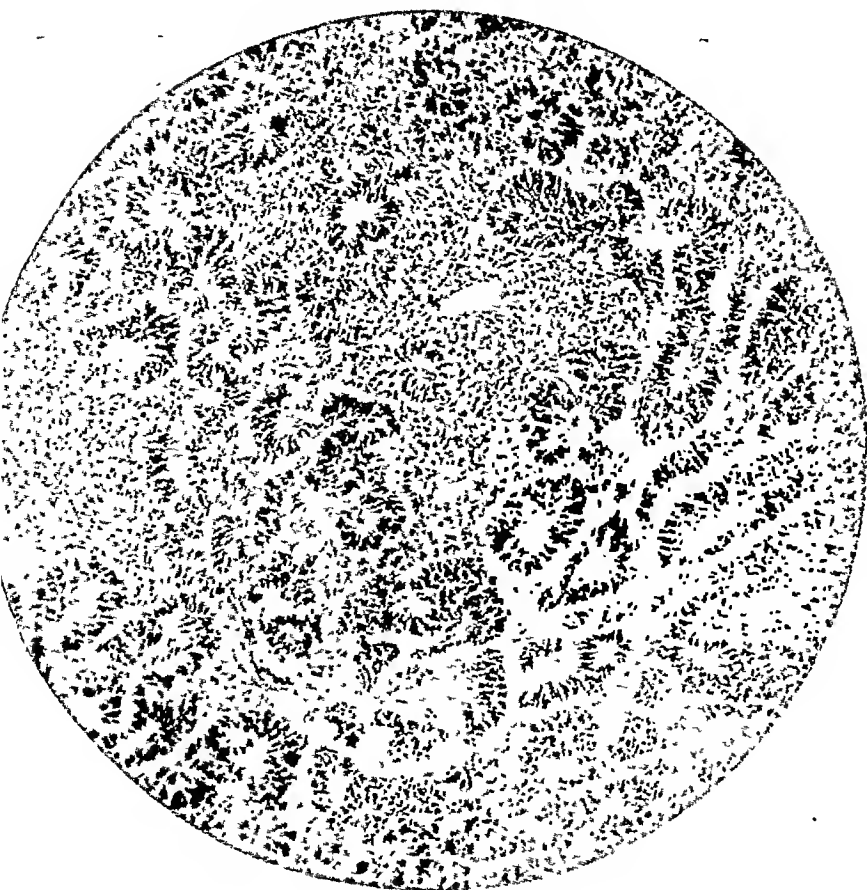
Fig. 12.—Case 3. Photomicrograph of the section from one of the thin cysts showing large cystic spaces. At the base note the dark stained angiomatous layer.



Fig. 13.—Case 4. Photograph of the tumour mass showing its position and size.



Fig. 14.—Case 4. X-ray picture of the area. Note the irregular scattered osseous tissue in the tumour mass.



ig. 16.—Case 4. Photomicrograph of a piece of the tumour mass showing the spindle cells taking a pseudo-alveolar pattern.

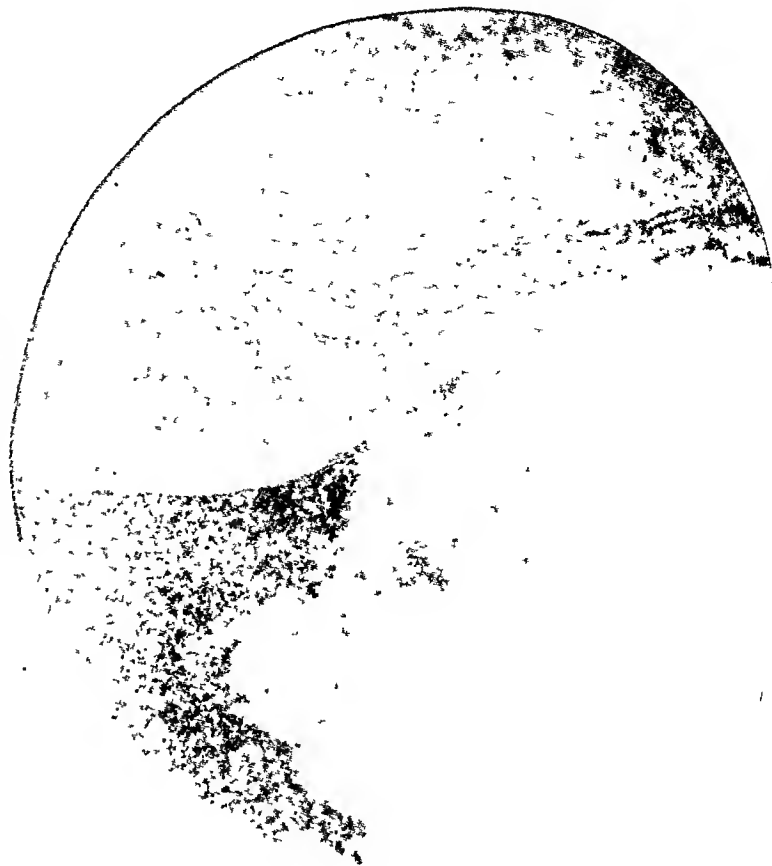


Fig. 17.—Case 4. Photomicrograph of the cross section of the vein showing solidly compact cells within the vein.

A CASE OF INTESTINAL INFESTATION WITH *HYMENOLEPIS DIMINUTA* IN
MAN : A. S. PARANDE. (M. H. P.) PAGE 256



Fig. 1.— $\times 600$.



100 μ
Fig. 2.

PLATE XLI
AN UNUSUAL CASE OF LYMPHOCELE OF THE SCROTUM : B. P. TRIBEDI.
(M. H. P.) PAGE 256



Coloured diagram of the specimen showing the uniformly fine granular appearance of the spherical bodies.

A CASE OF ACUTE TINGLING

By MADAN MOHON GHOSE, M.B. (Cal.)

Private Practitioner, P. O. Nakunda, Dist. Hooghly

ON 18th March, 1950, P. S., aged 35 years, of village Solepore, P. S. Goghat, district Hooghly, went to Arambagh—a distance of 6 miles away from his village, in the morning. He had taken some parched rice and water before starting.

In Arambagh at 10 a.m. he felt a little tingling sensation in his upper and lower extremities. One unknown person asked him: 'Why have you sat down?' The patient replied that he was feeling a tingling sensation in his hands and feet. The person told him to sit under the mouth of a tube well and he began to pump water. The patient felt a little relieved. The person called a motor car and requested the driver to carry him to his place. The car carried the patient 5 miles only. The patient came down and began to walk towards his home with trembling legs.

After reaching home at 3.30 p.m., the tingling sensation became more intense and painful. With this acute sensation he began to feel as if insects were biting him all over. He took a little 'Tari' (fermented palm juice) in the hope that the severity of the pain would be reduced but it became even more intense. He with the help of his two brothers began to walk towards my surgery, which was at a distance of 1 mile. At 4 p.m. I saw him coming crying loudly.

I examined him but the patient was violent, so a thorough examination could not be done. The patient was conscious. He was crying loudly saying that his hands and feet were bending and that many insects were biting him all over. Eight to ten persons were not able to keep him calm and quiet by holding him tightly. The pulse was feeble, the conjunctivæ were not congested, heart sounds were feeble, respiration was forceful, the hands and feet were bending, and the neck was rigid. The patient was crying loudly and becoming violent.

I asked some persons to pour water on his head constantly as ice was not available in this Nakunda village. I injected one ampoule of atropine sulph. 1/100 gr. intramuscularly but after 15 minutes no marked improvement was seen. The persons were pouring water constantly. Then I injected one ampoule of atropine sulph. 1/100 gr., et morphine sulph. $\frac{1}{4}$ gr. intramuscularly. After 5 minutes the patient became calm and quiet. Water was still being poured on him. After 30 minutes he said that he was feeling chilly. He sat down and said that he did not know when the persons were pouring water on his head, when and where I injected him and that his pain was less. I asked him to remain in my place for that night and to take two doses of medicine at night.

B

Pot. brom.	..	xv gr.
Chloral hydrate	..	vii gr.
Tr. vallerian ammon.	..	xx m.
Sodii bicarb.	..	xv gr.
Tine. card. co.	..	x m.
Syrup rose	..	30 m.
Aqua chloroform	..	5i

mist, send 2 such, six-hourly.

The next morning he stated that he had a feeling of heaviness and that there was practically no pain. The patient is now in good health. This condition is ordinarily called 'Ghingini'.

[For an epidemic of *Shin-jhinia*, another name for the same condition, see this journal, 71, pp. 91, 118 and 205—Edron, I.M.G.]

Therapeutic Notes

NOTES ON SOME REMEDIES

XXXIV.—DEHYDRATION AND ITS TREATMENT

By R. N. CHAUDHURI, M.B., M.R.C.P., T.D.D.

Department of Tropical Medicine, School of Tropical Medicine, Calcutta

Part V. Treatment of cholera

CHOLERA presents a picture of mixed salt and water depletion, its most outstanding feature being dehydration with consequent hæmoconcentration and peripheral circulatory failure. A patient may lose fluid enormously, and in very bad cases we have observed the plasma reduced as low as to one half its volume though the total blood volume was not markedly altered. Treatment consists mainly in replacing the lost fluid and salt, and giving alkalis for the acidosis which usually develops as a result of the electrolyte disturbance of the body fluid. These measures help in restoring the circulations and maintaining the functions of the kidneys, and recovery usually follows if the treatment is begun early enough.

Degrees of dehydration

This may be gauged from the following:—

(1) *Clinical condition*.—Generally speaking, the signs of severe dehydration are cold skin, diminished elasticity of the skin, sunken eyes, cyanosis of lips and nails, 'washer-woman's hand', great thirst, husky voice, scanty urine, imperceptible or very weak pulse and very low or not measurable blood pressure. These data will serve in assessing less severe degrees of dehydration.

(2) *Specific gravity of blood or plasma.*—This indicates the extent of fluid loss. The specific gravity of blood is estimated by glycerine and water mixtures or the copper sulphate method. The normal specific gravity is 1056 to 1058. The higher the specific gravity above this level, the greater is the loss of fluid that has taken place. A specific gravity of 1061 is taken as indicating an approximate loss of one pint of fluid, 1062 two pints, 1063 three pints and so on, and these amounts are required to replenish the losses.

Ghanem and Mikhail (1949) found the specific gravity of plasma a more reliable guide, because the specific gravity of blood is liable to vary. It can be easily estimated (copper sulphate method). The normal specific gravity of plasma (or serum) ranges between 1025 and 1028 and it rises in proportion to the dehydration as shown below:—

<i>Specific gravity of plasma</i>	<i>Dehydration grade</i>
1025-1030	+
1031-1040	++
1041-1050	+++

N.B.—The specific gravity of blood (or plasma) and the blood pressure should be estimated at appropriate intervals and the data thus obtained serve, in addition to the patient's general condition, as a measure of the results of treatment and as a guide to further treatment.

Fluids used

Rogers recommended *hypertonic saline* (sodium chloride 120 gr., calcium chloride 4 gr., water 1 pint) but some workers have obtained equally good results with *normal saline* (sodium chloride 90 gr. to a pint). Saline supplies the salt (total blood chloride is reduced though the chloride concentration may be high), but it seems that the loss of water is comparatively greater, for which normal saline is better indicated. Later when the chloride requirements of the body have been satisfied, *hypotonic saline* ($\frac{1}{2}$ to $\frac{1}{3}$ normal saline) should be used. Alkalis are given to combat acidosis—sodium lactate in mild or moderate cases and sodium bicarbonate when it is severe. *Sodium lactate* as 1/6 molar solution is effective; it can be boiled and used subcutaneously or intravenously. *Sodium bicarbonate* is used in 2 per cent solution (180 gr. to a pint) but in a higher strength, viz, 5 per cent (440 gr. to a pint), when uræmia develops. In preparing the solution, the sodium bicarbonate is first sterilized in packets and then added to the sterile water. It should not be boiled. Ampoules containing sterilized solution are convenient. Sodium bicarbonate should not be used subcutaneously nor should it be added to a solution containing glucose. As too much of alkalis is liable to cause alkalosis which in itself may affect renal functions, it is

desirable to determine the CO_2 content of the blood. But as this is not practicable in general practice, it is best to use a small quantity at a time in proportions mentioned later and follow it with more if the acidosis is not soon corrected. *Glucose* is a very useful adjunct in cholera treatment. It can be given orally with water or saline, and in 5 per cent solution is usually mixed with normal saline to make the latter hypotonic. In higher strength (20 per cent) it may be of value in cardiovascular weakness.

The amount of fluid needed

It is usual to be guided by the specific gravity of the blood which, as already stated, gives a clue to the degree of dehydration. But there can be no very definite rule in this matter. The patient's condition as determined by the history of frequency of diarrhoea and vomiting and by the clinical evidence of dehydration will also serve as a guide to the amount for parenteral therapy. The body weight too must be taken into account. Later, the sufficiency of the infusion must be judged by its effect on the patient's pulse, blood pressure and other signs and symptoms. It should be remembered that a cholera patient in the acute stage is in a continual state of flux due to drain of body fluid, not only with the stools and vomit but also through sweating (due to exhaustion and collapse) and hurried breathing (through circulatory changes and acidosis), and that even with suitable treatment constant changes are going on. The aim should be to secure adequate hydration without producing oedema. The amount of fluid needed to get an adult patient over the critical stage may range from 6 to 12 pints and further amounts will depend on his progress. In urgent cases two to three pints may be given immediately without wasting time on specific gravity and blood pressure measurements.

Management

As dehydration sets in rapidly and this in its turn brings in the complications, treatment should be started as early as possible. Every thing that is possible should be done to preserve the patient's strength. All unnecessary movements should be avoided and the patient must not be allowed to go to the latrine but use a bed-pan or have a rubber sheet placed under him where he can pass stools and which can be changed every now and then. He should be under continuous observations; one or two visits are not enough and there should be a reliable nurse to report changes in his condition which may develop with alarming speed. Overheating the patient is bad, a bedsheet or light blanket covering is enough in warm climate, and hot water bottles should not be used unless the temperature is subnormal.

✓ It is usually not necessary to give parenteral fluid if the pulse is fairly good, blood pressure

not too much reduced and the specific gravity of the blood up to 1060. Fluids by mouth (water, green cocoanut water, glucose in saline) are enough, but may be supplemented by subcutaneous saline. In other cases intravenous therapy must be used. The following are sufficient indications for such therapy—coldness of the extremities, restlessness and cramps; thready or imperceptible pulse and systolic blood pressure below 90 mm. Hg. The steps of the treatment may be summarized as follows:—

(1) Start with normal saline, but in cases with excessive vomiting the first two pints may be hypertonic saline.

(2) Run in the solution at first quickly and then more slowly: the first pint in 10 minutes (2 oz. per minute), the second in 15 minutes and the third in 20 minutes. If the patient complains of headache or oppression of the chest, reduce the rate of flow.

(3) Now continue the infusion by drip method—a pint in two to four hours (100 to 50 drops to a minute). Remember that bulky infusion given at a quick speed is dangerous when cardiovascular weakness is present.

(4) If the drip method cannot be employed, repeat the infusion in 2 to 3 hours.

(5) Collect the urine every 8 hours as far as possible and note the quantity, reaction and the amount of chlorides present in it.

(6) Continue the treatment on the above lines until the pulse and blood pressure are restored to near about normal, the specific gravity of the blood drops to about 1060 and the general condition improves. By this time he should be able to pass some urine, about 12 oz. in 8 hours, with 3 to 5 gm. of chlorides per litre.

(7) If parenteral fluid is still required, give hypotonic saline ($\frac{1}{2}$ to $\frac{1}{3}$ normal saline made up with glucose solution).

(8) If at any stage signs of acidosis are present, viz, air-hunger type of breathing, drowsiness and increasing restlessness, add sodium lactate solution to the saline or glucose and saline in the proportion of 1 to 2 or 3 parts. Continue it until these symptoms are relieved and the urine becomes neutral or slightly alkaline. If the symptoms are more pronounced, use sodium bicarbonate solution (180 gr. to a pint) with the saline instead and in the same proportion. Any of these alkalis may be used alone if there is no indication for saline.

(9) Even if there are no active signs of acidosis, it is advisable to use some alkali 24 hours after the onset of the illness to counteract the latent acidosis that often develops about this time. Early correction of acidosis appears to be of great importance in the subsequent course of the disease.

(10) As soon as the patient is hydrated, encourage oral intake of fluids. Even though vomiting may persist, by allowing an ounce or

two at a time with short intervals he will frequently retain a fair amount. Supplement oral intake, if necessary, with subcutaneous fluid.

(11) Be on the alert and watch for relapses when repeat the above treatment.

(12) To avoid over-hydration, frequently examine for pulmonary oedema.

(13) Keep a careful record of all relevant data on a sheet—temperature, pulse, respiration, blood pressure, stools, urine, laboratory findings, fluids, etc.

Not much information is available on the value of plasma or serum in cholera. Some claim it is specially useful in repeated collapse, giving a pint at a time, along with the saline. It has been found however that the blood proteins are markedly increased in cholera, as much as 10 gm. or more, and this seems to contraindicate its use.

With proper treatment the patient revives and his general condition improves. The diarrhoea gradually ceases and the stools regain their normal consistency. The vomiting ceases earlier than the diarrhoea. Recovery, once it starts, is usually quick. The diet should be cautious but need not be unduly strict:—

Diet in cholera

Stage	Feeds	REMARKS
Active (24-48 hours).	Plain water or half normal saline in sips. Alternative drinks— Green cocoanut water Soda water or Saline with glucose flavoured with lemon juice.	Saline and glucose infusions for dehydration and collapse.
Intermediate.	Barley, arrowroot or rice water with salt and sugar.	May add whey or buttermilk.
Convalescent.	Buttermilk and over-boiled rice. Salt and sugar are added.	Proceed cautiously: Soft rice, mashed green banana and potato, fish, dahi, etc.

Renal failure and uræmia

In the stage of reaction the acute symptoms disappear, the skin becomes warm to the touch, the diarrhoea diminishes and the urinary secretion increases. Recovery takes place within a week. However in unfavourable cases the urinary secretion does not return to normal. In such cases the pulse may become full and bounding and the systolic pressure increased, and if the renal failure persists, the patient passes into a state of uræmia which is usually associated with

a high degree of acidosis, so much so that even, after relatively large injection of sodium bicarbonate, the urine may remain sharply acid. This uræmia which is the result of retention of uræa and acid metabolites is the most serious complication in the late stages of cholera. It manifests itself more often as extreme fatigue, apathy, slow cerebration, muscular twitchings, nausea or slight diarrhoea, and only occasionally delirium, convulsions and coma are present. The anuria seems to be the result of renal anoxia from diminished blood flow leading to tubular changes and insufficiency of glomerular filtration. Treatment is directed towards acidosis and although this may not strike at the root cause of the trouble, it tends to correct the diminished alkalinity of the blood and eliminate the waste products by promoting diuresis. When the dehydration has been of long standing, there may not be any response to the treatment even after correction of the acidosis.

At the onset, give sodium bicarbonate, 2 to 3 drams, by mouth, small quantities at a time, or if gastric irritation is present, by rectum either by drip method or every few hours. If the uræmic symptoms are more urgent, give it by vein, using 5 per cent solution (440 gr. to a pint), half a pint at a time and follow it by mouth or rectum, if possible. When the kidneys begin to secrete freely, reduce the concentration of the alkali and stop it altogether as soon as possible. Diuretics are contra-indicated.

In acute renal insufficiency it is important not to force too much fluid, as the resultant œdema may embarrass rather than encourage the return of renal function. It should be just enough to cover the losses, *viz.*, about 1,000 cc. (for normal loss through the skin and lungs) plus what is lost with the vomit, stools and urine (if any), and say about 500 cc. to supply the volume for urine. This is made up partly by the alkaline solution mentioned above and partly by barley water, whey, buttermilk and sweetened drinks like tea, orange juice and glucose (with water soluble vitamins). It is also important that fluids by vein should be minimum. When the kidneys are out of action, oral intake ensures better adjustment of water-salt balance. It also keeps the patient from heart strain to which he is liable at this stage if fluids are given by vein. No sodium chloride should be given in complete anuria except to replace what is lost with stool and vomit when a weak hypotonic solution should be enough. As diuresis occurs, fluids and salt should be proportionately increased.

Drugs in cholera

(1) *Sulpha drugs*.—There is no unanimity as to their efficacy in cholera. Some workers have obtained good results with *sulphaguanidine*, 2 gm. *stat* plus 1 gm. 2-hourly, it should be continued until the diarrhoea is well controlled.

Sulphadiazine is not recommended owing to the hazard of urinary complications. A new compound (formo-cibazol), prepared in India by Bhatnagar *et al.* (1948), is under trial. A total dosage of 28 gm. is given—10 gm. on the first day, two doses of 4 gm. on the second day and two of 1 gm. each morning and evening every subsequent day for 5 days. It may also be used prophylactically. But chemotherapy can in no way replace the use of saline infusion which is necessary for combating dehydration and collapse during the acute stage.

(2) *Chloromycetin (chloramphenicol P. D.)*.—Recently in collaboration with Dr. S. Ghosal, Professor of Bacteriology and Pathology, 10 bacteriologically positive cases of cholera were treated with chloromycetin which was shown by Gauld *et al.* (1949) in *in vitro* experiment tests to inhibit completely the growth of *V. cholera*. Alternate cases that were admitted served as the control. All were admitted within 5 to 14 hours of the onset of illness and had received no previous treatment. The drug was given by mouth in divided doses, 24 capsules (0.25 gm. each) on the first day, and 12 capsules each on the second and third days, altogether 48 capsules in 3 days. It was started usually after the first saline infusion and when the reaction, if any, was over. Any dose vomited within half an hour was repeated after a short while. Fæces of each patient obtained by passing a catheter were examined daily. General management including saline treatment was practically the same in the treated as well as control group. No obvious clinical difference was observed between the two groups. Rapid disappearance of vibrios from the fæces was however remarkable in those who had the drug; the number of colonies was reduced to insignificant number in 24 hours and nil by 48 hours, while vibrios were isolated from the control patients for a period up to 7 days. This indicates that it may have a prophylactic value during epidemics and possibly exert some influence on the course of the disease by quickly getting rid of the bacteria. Further trials are advisable.

(3) *Other drugs*.—*Pituitrin* may be given if the blood pressure is persistently low; atropine sulphate for prevention of pulmonary œdema. Suprarenal cortical extract, coramine or cardiazol may be useful during collapse stage or in cardiovascular weakness persisting after the patient is hydrated.

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Indian Medical Gazette

JUNE

AGAINST PESSIMISM IN TUBERCULOSIS

In aid of a flag day, organized by the Tuberculosis Association of Bengal, an appeal in the daily press read as follows :

A flag day in aid of the Bengal Tuberculosis Association will be observed in Calcutta to-morrow. The Association, it is stated, is responsible for 14 clinics in Calcutta and the mofussil, where about 95,000 cases are annually examined and some 5,000 cases of tuberculosis diagnosed and treated free. It gives x-ray facilities to indigent patients attending the clinics. The annual income of the Association is about Rs. 50,000. An appeal has been issued to the public for funds to enable the organization to carry on its useful activities (*Daily Press*, 1950).

The news appeared to be too good to be true. The suspects appeared to be only about 5 per cent.

The news appeared to be too good to be true particularly in contrast with :

'In recent years there has been a growing tendency to develop the dispensary unit into chest clinic A further argument in support of the change is that a high proportion of the cases referred to the dispensary for diagnosis are not suffering from tuberculosis. In one dispensary the average diagnosed as tuberculous was only 30 per cent of all new cases' (Heaf and Rusby, 1948).

On going into the matter further it was discovered that the real state of affairs was given by the following table :

suffering from tuberculosis has not increased significantly, except in 1948, in spite of an increase in the population of Calcutta, which has been for several years at least double of what it was in 1939. This is again good news. (3) The positive figure has not increased significantly in spite of the hardships of life in the town. The hardships have increased steadily since 1939 and acutely since 1947. (4) The positive rate has decreased significantly at least in 1948. All this is still good news.

The best news became available the other day from an academic source. Here it is : In a rural area out of 657 subjects tested with tuberculin only 11.8 per cent were positive; and in another rural area out of 826 subjects 11.5 per cent were positive. In the combined population of 1,483 subjects there were only 5 active cases of tuberculosis (personal unpublished communication). Rural population which is India appears to be all right. The trouble arises when the greed of cash brings it to the foci of industry. Then it sickens and dies of any disease that is going. Tuberculosis is only one of the diseases. In 1948 all deaths from plague in hospitals in Calcutta occurred among non-Calcutta labourers. The victims really died of discomfort and deprivation. So they do when they contract tuberculosis. In the early days of development of railway workshops they died of malaria at Saharanpur.

We have written previously on incongruities in tuberculosis (Editorial, 1948a). The following points are repeated : (1) The tale of tuberculosis opens like *A Tale of Two Cities*. 'It was the best of times, it was the worst of times . . . ' (2) Public health and medical relief measures are reducing the incidence of tuberculosis : and (2a) Public health and medical relief measures are not essential for the decrease in the incidence of tuberculosis. (3) Increase of tuberculosis in the war-ravaged Europe : and (3a) No increase in tuberculosis in the war-ravaged Europe. (4) Tuberculosis may be leaving the European stock alone but it still takes its toll of the non-European races : and (4a) Tuberculosis has declined in the non-European population of New Zealand. (5) Immunization with BCG discouraged : and (5a) Immunization with BCG

	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948
New cases	12,283	12,987	13,317	4,727	4,823	7,572	12,169	13,993	14,346	21,412
Diagnosed pulmonary tuberculosis.	3,599	4,025	4,338	2,053	2,124	2,738	3,542	3,805	4,076	4,620

(Extracted from The Bengal Tuberculosis Association, Annual Report, 1948)

The following conclusions emerge : (1) The positive rate. It is 21 per cent for the last year in the report and when compared with the figure from a British clinic it is still good news. (2) The number of patients who think they are

encouraged. (6) Streptomycin treatment discouraged : and (6a) Streptomycin treatment encouraged. The discouragement almost amounted to a threat. The drug-resisting bacilli, it was asserted, would exterminate the

human race. (7) A comparison with the situation in Spain. More tuberculosis is being detected because of better facilities and most of the disease is occurring centripetally round foci of industry. (8) Tuberculosis in cattle in India. It is not a problem at all and is definitely much less than in Europe. It waned centuries ago. It is not likely to be waxing in humans now. (9) Tuberculosis in laboratory animals. It is definitely less aggressive than in Europe. Again, it is not likely to be more aggressive in humans. (10) Housing and feeding the industrial worker. Alimentation is the primary need of man and selective alimentation the primary joy of living of which are born strength, stamina and resistance to disease. Subsidized food and fuel from the countryside should be made available to the labour sojourning in towns. (Dishes prepared by simmering, done on fuel available in the countryside, cannot be prepared satisfactorily by the same population in towns, on fuel available in towns.) (11) A change in the outlook of the toiling millions. It should be stated bluntly that in our country no public health measures will succeed unless the outlook of the masses on life changes. Standard of living must be raised. This can be done more by social reform than by medical relief. (12) Diabetes of wealth. This is our national disease. As a diabetic hankers after carbohydrates so do the masses after cash. They are both unable to utilize the object they may secure. The carbohydrate passes out and produces ketosis. It may even kill. The cash is hoarded for a while and then squandered on births, deaths and marriages or on building a house of burnt bricks when one of unburnt bricks will do as well. It does not raise the standard of living. On this item we will say more on a later date.

The comparatively benign nature of tuberculosis in India attracted the attention of investigators in India fifty years ago. It was believed to be on the decrease then. A letter from an issue of this journal dated June 1900 appears in the present issue (p. 271). Let all those frightened by the flag day read it. It will dispel their fears and save their money.

Somehow or other in the last decade the tuberculosis scare so overpowered the medical profession that all ill-health and excessive mortality in special localities was attributed to tuberculosis. Even occurrence of kala-azar in unsuspected zones remained unrecognized. Such was the occurrence in the eastern districts of the United Provinces (Prasad, 1949). We added a note inviting attention to the blunder caused by the scare and persuading the frightened to cast off fear.

The pessimistic attitude of the Tuberculosis Associations in this country is likely to defeat their humanitarian purpose for 2 reasons: (1) Available funds will be spent on old schemes which will remain utterly inadequate. Special sanatoria and dispensaries cannot be built for

the teeming millions. (As a matter of fact they are not required really on the scale demanded.) Besides, these measures are not succeeding in the West. (2) New schemes will not be tried. Such schemes are special settlements such as the Papworth Settlement. In this settlement infected husbands and wives have bred children who have remained healthy.

'Of 151 children admitted in families with positive sputum, 37 presented no clinical or radiological evidence of tuberculosis; 101 showed evidence of past infection; 4 had juvenile tuberculosis and 9 developed pulmonary tuberculosis of the adult type (adult phthisis). All were ten years of age or over on admission to the settlement' (Macnalty, 1944).

'Of 108 children born in the village, as many as 55 presented no clinical or radiological evidence of tuberculosis; 53 showed evidence of past infection.' The findings of the years, 1926, 1927, 1932 and 1933 already quoted are confirmed by additional years of experience. None of the village-born children (and more have now come of age) has, while a member of the community, contracted tuberculosis of the lungs, glands, bones or joints, or, indeed, in any known clinical form'. . . . 'These are remarkable results'.

The infectivity of the germ is not of a high order. More often than not it spends almost a life of symbiosis in the host and then dies out. Given comfort, good food and freedom from worries of life, cases of tuberculosis can live and work, and bring up healthy children almost like normal men and women.

Such schemes will produce even better results in our country than they have produced in the West. For some reason or other tuberculosis does not thrive here unless the infection is massive and the living conditions particularly hard. Such a combination is found in the slums of foci of industry. Greed of cash brings a lad from the farm to the factory or to slums in towns, as a factory worker or a camp follower of industry. He lives with others in utterly inadequate dwellings and cannot have his usual food. The joy of living and stamina to resist infection desert him. He dies of any disease going. Tuberculosis, as has been said before, is only one of the diseases. In 1948 in the recrudescence of plague in Calcutta he died of this disease (Editorial, 1948b).

Some problems well worth the consideration of the epidemiologists are: (1) What makes our cattle, or even laboratory animals, resistant to tuberculosis? (2) What makes our rural population tuberculin-negative? (3) Is a mechanism other than acquired resistance at work? (4) Are our soil, light and air inimical

to *Mycobacterium tuberculosis hominis* and *Myco. bovis*? (5) Is tuberculosis not a dying disease?

Dwelling on what we have read, seen and written has made us quite optimistic on the question of tuberculosis, in spite of the assertions to the contrary by the Tuberculosis Associations and in view of recent advances in chemotherapy resulting in the introduction of the less toxic streptomycin and of PAS (Editorial, 1950).

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Medical News

ROSS INSTITUTE OF TROPICAL HYGIENE : COURSE IN TROPICAL HYGIENE FOR PLANTERS AND MINERS. TO BE HELD FROM 24TH TO 28TH JULY, 1950

The annual course for laymen will be held by the Ross Institute this year from Monday, 24th July to Friday, 28th July, inclusive.

Last year's course, the first held since the war, was very successful and was attended by 65 students. A number of appreciative letters have since been received from students, and from companies from which they came. Well over a thousand planters and miners, etc., have now been trained since these courses were instituted.

The courses are arranged so that the morning sessions provide a continuous course on malaria and its control, and in the afternoons other tropical diseases and problems are dealt with, such as hookworm, bilharzia, nutrition, housing and sanitation, and protection against heat.

There is no fee for the course. It would be appreciated if agencies and firms would inform their managers and assistants that the course is being organized and encourage and assist to attend.

The names of those proposing to attend should be sent as soon as possible to the Organizing Secretary, but amendments and additions may be made at any time up to the date of commencement of the course.

Further information of the detailed arrangements and syllabus will be sent to those attending about a month prior to the date of the course.

L. G. PONSFORD,
Organizing Secretary.

28th February, 1950.

DRAFT STANDARDS FOR SULPHURIC, HYDROCHLORIC, NITRIC AND BORIC ACIDS.

(Reproduced from a release issued by Press Information Bureau, Government of India, New Delhi, 12th April, 1950)

SULPHURIC acid, hydrochloric acid, nitric acid and boric acid are of basic importance in the manufacture of other chemicals, drugs, fertilisers, textiles, paper and a number of major and minor industries. India is now producing substantial quantities of these for various purposes. Some of these acids are required in different grades for use in different industries. The Indian Standards Institution has, therefore, drawn up four separate draft Indian standard specifications for sulphuric acid, hydrochloric acid, nitric acid and boric acid.

The standard for sulphuric acid covers the technical, battery, pharmaceutical and analytical reagent grades. The standard for hydrochloric acid covers the technical, pharmaceutical and analytical reagent grades. The standard for nitric acid covers the grades for technical, nitration, pure and analytical reagent acids.

These specifications prescribe the minimum content of the acids and their specific gravities. The limits for residue on evaporation, iron oxidizing impurities, heavy metals (lead), arsenic and other insoluble impurities have been fixed. Clauses relating to containers, method of packing, marking and sampling of the acids are also included. The procedures to be employed for examination of these materials for conformity to the prescribed requirements are provided in the form of appendices in each standard.

The draft Indian standard specification for boric acid (commercial) prescribes the acid content of the material, the limits for free moisture and soluble iron compounds. For the material intended for use in electrolytic condensers, the limits for chlorides, sulphates and heavy metals are also included. The method of sampling and analysis of boric acid are included in the standard in the form of two appendices.

These drafts have been circulated to members of the Institution interested in this field and to large consumers, manufacturers and technologists concerned. Comments on these draft standards will be received by the Director, Indian Standards Institution, 19, University Road, Delhi 2, up to 20th June, 1950.

THE USE OF STREPTOMYCIN : REPORT PUBLISHED BY THE EXPERT COMMITTEE OF THE WORLD HEALTH ORGANIZATION

(Issued by the Tuberculosis Association of India, New Delhi)

THE USE OF STREPTOMYCIN

It is emphasized that streptomycin, while being useful in the treatment of several forms of tuberculosis, is, at its best, only a part of the general treatment in most forms of the disease and is partially dependent for its full effect upon other more common therapeutic measures, such as bed rest, pneumothorax or chest surgery. It is generally known that even under the best therapeutic conditions, severe toxic manifestations occur, some of them fairly frequently. Furthermore, tubercle bacilli in certain patients acquire resistance to streptomycin which eventually necessitates termination of specific therapy. It was, therefore, recommended that during the initial period of study and use streptomycin should be distributed by governments only to institutions and medical centres regularly concerned with the diagnosis and treatment of tuberculosis. With such safeguards, limited supplies will be beneficially employed under the supervision of physicians experienced in streptomycin therapy, aware of its dangers and contraindications and prepared to carry on further research on

the more precise use of this and other newly developed antibiotics against tuberculosis.

TYPE OF CASES SUITABLE FOR TREATMENT

Streptomycin was not found to be suitable for all types and stages of tuberculosis infections.

It was unanimously agreed that patients with tuberculosis meningitis and generalized hematogenous or miliary tuberculosis should be given prior consideration, because of the extremely high mortality-rate among untreated cases and the lack of any other dependable therapeutic approach.

It appeared that fulminating types of broncho-pneumonic pulmonary tuberculosis of recent origin, which have not progressed beyond the possibility of healing, may frequently be ameliorated by streptomycin; residual lesions of a more chronic and destructive character may require other forms of treatment.

Some of the most distressing complications of pulmonary tuberculosis, especially tuberculous laryngitis and tuberculous enteritis, may be greatly benefited symptomatically by appropriate streptomycin treatment.

Finally, streptomycin was found to be particularly effective in the treatment of tuberculous sinuses and fistulae; less favourable results have so far been reported in renal tuberculosis and in tuberculosis of bones, joints and glands.

REGIMENS OF TREATMENT

Optimum streptomycin regimens for the different forms of tuberculosis have not been determined with sufficient precision to make exact recommendations possible at this time. At the present stage of knowledge, the medical practitioner cannot expect to be provided with a universally accepted formula, but will have to make his own choice from several regimens recommended by various research workers.

The group of experts could therefore hardly do more than define certain general principles to be observed in the application of streptomycin therapy. Thus, it was suggested, among other things, that in certain cases when the disease changes for the worse or when a relapse occurs, a subsequent or second course of streptomycin may be indicated, provided that the tubercle bacilli have not become predominantly streptomycin-resistant. The indications for a second course of treatment cannot, in the present state of knowledge, be specified precisely, but must be determined after careful review of all clinical and laboratory data in each case. There was, in the opinion of the group, some evidence that combined therapy (streptomycin plus sulphone derivatives or para-aminosalicylic acid) may be more effective in some forms of tuberculosis than either drugs used alone. At the present time, combined therapy shows greatest promise in the treatment of miliary tuberculosis and tuberculous meningitis.

APPENDIX

In continuation of the recommendations given in the above report the Expert Committee of the World Health Organization at its Fourth Session in Copenhagen from 26th to 30th July, 1949, further recommended that attention be drawn to the inadvisability of the unrestricted distribution and indiscriminate use of streptomycin for the following reasons:—

- (1) In spite of reduced toxicity of new forms of streptomycin, the drug must still be regarded as having danger.
- (2) Lack of precise knowledge as to its clinical indications, especially in pulmonary tuberculosis.
- (3) The focusing of attention of the public on this drug out of all proportion to its value in the total campaign against tuberculosis.

BRITISH SURGEONS INVITED TO YUGOSLAVIA

Two British experts in plastic surgery and anaesthesia, Mr. Rainsford Mowlem of the Plastic Unit of Middlesex Hospital, and Dr. Woodfield Davies of the Postgraduate Medical School, London, are now on a visit to Yugoslavia, at the invitation of the Yugoslav Ministry of Health, lecturing on techniques of Plastic Surgery. British plastic surgeons gained an enviable reputation as a result of the remarkable work they performed during the war on men whose wounds and injuries were so dreadful that it seemed almost impossible that they could ever take their place in the world again.



Two patients consulting the surgeons at a London Hospital.



THE NEW SURGICAL NYLON DRESSING FOR WOUNDS

Exhaustive tests at an engineering works near Manchester, England, have indicated that wounds treated with this type of dressing tend to heal more quickly than those covered by waterproof dressings more normally used for industrial injuries. Note the transparent window in the dressing which allows examination of the wound.

REGISTER OF SCIENTIFIC PERSONNEL : 'ENGINEERS' VOLUME PUBLISHED

(From a release dated 4th May, 1950, issued by Press Information Bureau, Government of India)

THE initial volume of the National Register of Scientific and Technical Personnel in India—published by the Council of Scientific and Industrial Research—includes the names of engineers under various categories, such as civil, electrical, mechanical, chemical, marine and mining. These have been put into categories in which the personnel are considered to be specialists. The information furnished is classified under various sub-heads, such as academic and professional qualifications, practical experience—its nature and scope—present and permanent address, present occupation and nature of employment held.

It is expected that a series of volumes will soon follow covering other categories of scientific and technical personnel, such as chemists and chemical technologists, physicists, doctors, metallurgists, agricultural scientists, biologists, geologists, zoologists, dairy scientists, foresters, mathematicians and statisticians.

SCIENTIFIC MANPOWER CENSUS

A positive effort towards the stock-taking of scientific personnel in the country, the National Register should also serve as a pre-requisite for assessing, qualitatively and quantitatively, India's manpower resources and formulating plans for the training of personnel required for economic development and research. Periodically revised and brought up to date, it is expected to provide a continuous census of scientific manpower and to be of assistance in the effective utilization of scientific talent, assessing gaps in the growth of science and technology, supplying service personnel to industry, finding alternative personnel in the prosecution of team work, and provision of personnel for educational and research institutions.

The proposal to undertake a census of scientific and technical manpower was made by the Scientific Man-

power Committee, appointed by the Government of India in 1947 under the Chairmanship of Dr. Shanti Swarup Bhatnagar. The work was assigned to the Council of Scientific and Industrial Research which, in co-operation with the National Institute of Sciences of India, called upon the country's scientists, engineers, technologists, doctors and others to register themselves in the National Register. The Prime Minister also urged the public to respond to the call for registration.

To facilitate the collection and compilation of information for the National Register, a suitably devised questionnaire has been issued, and the Council hopes that scientists and technicians who have not yet registered will supply the needed information, so that this national undertaking may be completed satisfactorily and expeditiously.

MENACE OF THE 'DUSTED' LUNG : WORLD EXPERTS MEET AT SYDNEY

By C. C. D. BRAMMALL

(Reproduced from Release No. P/1428, issued by the Public Relations Officer, Australian High Commissioner's Office, Connaught Place, New Delhi)

WORKERS would be protected against exposure to the risk of contracting dust diseases of the lungs if methods of dust suppression and control now in existence were fully applied and maintained.

This was one of the findings of the third international conference of experts on pneumoconiosis—dust diseases of the lungs—convened in Australia by the International Labour Office. The conference recommended that every effort should be made to apply these methods.

Physicians, physicists and industrial engineers drawn from 12 countries, all specialists in pneumoconiosis, attended the conference, which took place in March in the School of Public Health and Tropical Medicine at the University of Sydney.

They agreed that the work of the engineer in dust suppression and prevention is of such vital importance that another conference should shortly be called by I.L.O. at which engineers and physicists interested in the subject should predominate.

Australia has been a prominent member of I.L.O. since 1919, and has been represented at all conferences since that time. She has been a member of the Governing Body—the executive of I.L.O.—since 1945.

Australian representatives attended both previous conferences of experts on industry-caused dust diseases of the lungs held at Johannesburg, South Africa, in 1930, and at Geneva in 1938.

Dr. W. E. George, Chief Medical Officer of the Joint Coal Board (Australia) was present at both. He was unanimously elected chairman of the Sydney conference.

Experts from Australia, Canada, Denmark, France, Italy, the United Kingdom, New Zealand, Norway, Sweden, Switzerland, the United States of America and the Union of South Africa were present. There was a delegation of two Australian members of the Governing Body in Mr. F. J. R. Gibson and Mr. A. Monk.

In addition, five experts appointed by I.L.O. attended in Dr. George, Professor C. E. Gernez-Ricux (France), Dr. E. L. Middleton (United Kingdom), Dr. A. J. Orenstein (South Africa) and Dr. A. J. Vorwald (U.S.A.).

A fundamental definition of pneumoconiosis was adopted by the conference. This declared that it is a 'diagnosable disease of the lungs produced by the inhalation of dust, the term dust being understood to refer to particles of solid matter, but excluding living organisms'.

Discussions took place on how pneumoconiosis is caused, diagnosed and treated, how it can be prevented, the effects of different dusts on the lungs, and the possibility of defining minimum international standards of compensation for disability caused by dusting.

Dr. George said at the conclusion of the conference that in his opinion the most important part of the discussions, which included the reading of more than 30 papers by the experts attending, dealt with the prevention of pneumoconiosis in the future.

'If pneumoconiosis can be prevented', said Dr. George, 'discussions on other aspects of the disease become of academic interest only.'

'Industry is becoming more health-conscious, and workers realize that the protection and maintenance of their health is far more important than compensation for injury to their health.'

'To industries with a dust hazard, I would say that ultimately it depends on the conscientious and continuous application of dust control measures by all those immediately concerned whether or not harmful quantities of dust will be present from time to time in the working atmosphere.'

'Engineers can provide the various methods for dust control. It is up to the employer and the worker to use them continually and conscientiously if pneumoconiosis is to be prevented.'

Conference agreed that the attention of governments, public utility corporations, local authorities and contractors should be called to the occurrence of silicosis following relatively short exposure to dust in civil engineering undertakings such as tunnelling and excavations.

It was pointed out that dust conditions may be so bad in some cases that although a worker's exposure to dust is comparatively short, its effect on him may be dangerous and the authority employing him may be unaware of the danger.

Even comparatively harmless dusts when present in quantity can be a menace. Others are harmful even in small quantities.

Conference also agreed that the protection of the worker might include such measures as:—

- Abolition of the process creating harmful dust;
- Substitution of harmless material in certain processes where dangerous material is being used;
- Suppression of dust at the source;
- Removal of dust as near as possible to the point of origin;
- Reduction of the concentration of dust by ventilation;
- Removal of dust from the air by wetting;
- Precipitating the dust by electrical methods;
- Personal respiratory protection to the worker.

But the opinion, expressed at previous conferences, was reaffirmed that the main efforts at prevention should be directed towards dust suppression and control, and that personal protection—for example, by using dust masks—should only be used wherever these suppression and prevention methods could not be put into operation.

Changes as they develop in the lungs of workers in industry were studied, and conference compared the different x-ray and clinical signs which different kinds of dust produce, discussed the standards for the assessment of disability and of compensation in different countries, and the possibility of the rehabilitation of the worker suffering from pneumoconiosis.

The importance of the consideration of three factors—the history and conditions of exposure to harmful dust, the clinical examination and the x-ray findings—was stressed. It was emphasized that the diagnosis of pneumoconiosis must not rest solely on the x-ray; that appearances on a radiograph are not necessarily related to the severity of the disease.

It was recognized that infection, especially by the tubercle bacillus, frequently complicates pneumoconiosis and aggravates of disability caused by it. Attention was drawn to the necessity for excluding tuberculosis cases from dusty occupations, and to the value of good hygiene and nutrition.

An outline of the medical examination system now in use in New South Wales by the operation of the Joint Coal Board medical bureaux was given at an illustration of how this might work.

It was decided that each country should define the conditions for compensation to workers diagnosed, as suffering from pneumoconiosis, and that these should be such as to ensure that compensation should be made available to each sufferer irrespective of the time which had elapsed since he had been exposed to dust.

It was agreed that where a worker was forced to leave his accustomed employment because of a pneumoconiosis diagnosis, every endeavour should be made to place him immediately or train him for suitable employment which would not reduce his standard of living.

Provision of such alternative employment should not prejudice the amount of his compensation.

A report of the findings of the conference will be made to the Governing Body of I.L.O.

The Governing Body, after considering the recommendations and discussing the whole problem dealt with by the conference, will then make recommendations to the governments which are represented in the organization.

Papers read at the conference by the experts who attended, together with verbatim reports of all discussions, will be published in book form by the International Labour Office. The resulting volume is likely to become a textbook on the subject, and will be available for the guidance of all confronted with a dust problem until the next conference is held.

[The following 6 items are reproduced from releases issued by W.H.O. Regional Office for S.-E. Asia, New Delhi]

I. MALARIA CONTROL IN CEYLON

REDUCTION TO 'INSIGNIFICANT IMPORTANCE' AN ATTAINABLE GOAL

(SEA/PR/50-23, dated 27th April, 1950)

Dr. BRUCE WILSON, who has just terminated a visit to Ceylon as W.H.O. Malaria Consultant, believes that malaria on the island can be further reduced to the point where it will be of 'insignificant public health importance'. This goal can be attained, says Dr. Wilson, in a very short time given full co-operation from the public and provided that certain improvements are made in the organization and technique of the existing anti-malaria services.

Ceylon may well be proud of its progress in fighting malaria during the last 3 years, declares Dr. Wilson. Official statistics put at his disposition showed that deaths attributed to malaria in 1949 were only a quarter of the figures for 1946. In 1949, however, one person in ten was still attending at dispensaries and hospitals for malaria treatment. Allowing for a considerable margin of error in diagnosis, malaria must, in Dr. Wilson's opinion, still be considered as a disease of first-rank importance in Ceylon.

At the request of the Ceylon Government, Dr. Wilson is at present preparing a report based on his observations during the 2½ months he spent in Ceylon. In this time he covered 2,800 miles and visited more than 50 localities in all parts of the island.

Dr. Wilson, who is on loan to W.H.O. from the International Health Division of the Rockefeller Foundation, was asked to advise on the possibility of total eradication of the malaria-carrying mosquito in the island. In his report, which will be submitted to the Regional Director of W.H.O. for S.-E. Asia and forwarded by him to the Ceylon Government, Dr. Wilson will therefore make a close study of the pros and cons of this question. One important consideration would seem to be the fact that the one species of mosquito at present known to carry malaria in the island has at times been found breeding in inaccessible jungle regions.

Further education of the public concerning the vital importance of the anti-malaria campaign is essential, in Dr. Wilson's opinion. In the past the public has on the whole co-operated satisfactorily. The campaign cannot however be expected to succeed if owners shut up their houses on the day of the spraying team's visit or refuse to permit all their rooms to be sprayed. Among the possibilities to be examined in his report is the extension of training facilities for malaria workers to include a course in propaganda techniques.

The report will also deal with the organization of the national anti-malaria service, and will suggest how W.H.O. can most usefully assist Ceylon in intensifying its malaria control programme.

Dr. Wilson is scheduled to leave New Delhi next week for Cairo to await his next assignment from the Rockefeller Foundation.

II. CZECHOSLOVAKIA WITHDRAWS FROM W.H.O. DESPITE ON-GOING PROGRAMME IN THE COUNTRY

(SEA/PR/50-24, dated 1st May, 1950)

A NOTE issued from the Geneva Headquarters of W.H.O. last week to announce the withdrawal of Czechoslovakia from the Organization lists the services

rendered by W.H.O. to Czechoslovakia since 1947. The list includes assistance in national campaigns against tuberculosis and against venereal disease, and the allocation of 62 fellowships to senior medical personnel of the national health administration for study in other countries including the Soviet Union. A grant of \$37,000 was made available to Czechoslovakia for fellowships in 1950. In addition to providing considerable quantities of medical literature and teaching equipment, the note goes on, W.H.O. has assisted the Czechoslovak government in the following undertakings:—

- (1) Establishment of a new State Medical Library and Documentation Centre: W.H.O. provided complete equipment for microphotography, subscriptions to 170 foreign periodicals and journals, and several collections of medical textbooks. A large part of this material has already been received in Prague, the rest is awaiting shipment.
- (2) A Training Centre in Anaesthesiology: W.H.O. is in the process of equipping this centre to provide international courses in modern techniques of anaesthesiology which has opened new fields to surgery in recent years. An agreement has recently been signed between W.H.O. and the Czechoslovak government, concerning the centre which was expected to open next month and to admit physicians from neighbouring countries.
- (3) Surgery and treatment of congenital heart diseases: A group of prominent Swedish scientists is scheduled to visit Czechoslovakia in June this year, under W.H.O. auspices, to demonstrate to physicians new methods of treatment for congenital heart diseases and more especially surgery techniques for operations on 'blue babies'. In addition to staff, W.H.O. has provided for complete diagnostic and surgical equipment, now ordered and almost ready for shipment.

Czechoslovakia is the seventh State to withdraw from the World Health Organization since it officially came into existence in 1948. The other six are: Union of Soviet Socialist Republics, Ukrainian SSR, Byelorussian SSR, Bulgaria, Roumania and Albania. As the W.H.O. Constitution makes no provision for withdrawal of Member States, the whole question of the status of these seven Members will be considered at the third World Health Assembly which will open in Geneva on 8th May.

III. 6,000,000 DOLLAR INTERNATIONAL PRO- GRAMMES FOR HEALTH IMPROVEMENT IN ASIAN COUNTRIES

(SEA/PR/50-25, dated 1st May, 1950)

PLANS for the expenditure of a sum of nearly six million dollars made available by the United Nations International Children's Emergency Fund for health improvement projects in Asian countries from Afghanistan to the Philippines were discussed in New Delhi this week-end between Mr. Maurice Pate, Executive Secretary of UNICEF, Dr. C. Mani, Regional Director of W.H.O. for South-East Asia, and officers and experts from both organizations. The meeting was a continuation of discussions begun at the UNICEF Far-East Headquarters in Bangkok earlier in April.

Many of the projects discussed have now received the technical approval of W.H.O. and have been cleared with the respective national governments who are required to make 'matching' contributions in each case. They now only await formal acceptance by the Executive Board of UNICEF scheduled to meet on 19th June. In some cases recruitment of personnel and the ordering of necessary supplies have already been begun.

Among the UNICEF/W.H.O. projects which are expected to go into operation before the end of 1950 or early in 1951 are the following :—

Afghanistan.—A combined training and demonstration programme designed to build up local services in maternity and child welfare and in the diagnosis and treatment of venereal diseases.

Burma.—Personnel, equipment, supplies and supplementary food urgently needed to launch programmes in school health, nursing training, and laboratory services. This is intended to be the first phase of an integrated maternal and child health programme to be developed subsequently. In addition personnel and supplies will be provided to upgrade existing anti-tuberculosis services in Rangoon.

British North Borneo.—Supplies to enable a maternal and child health programme to be launched. A team of W.H.O./UNICEF nursing experts are already at work in Sarawak and Brunei.

India.—Three tuberculosis training centres to be developed in Patna, Delhi and Trivandrum; assistance in developing a two-million dollar maternity and child welfare training project in conjunction with the All-India Institute of Hygiene and Public Health, Calcutta; an additional feeding programme in Indian schools; and the extension of the existing W.H.O. Maternal and Child Health Centre in Delhi province.

Indonesia.—It is proposed to sponsor and support with supplies and personnel a vast national programme for the control of yaws. The UNICEF contribution of one million dollars together with the Indonesian government's matching contribution is expected to provide treatment facilities for yaws sufferers among a population of 12,000,000 people. In addition it is proposed to equip several nurse-training centres and to provide supplies for a number of polyclinics and maternal and child health centres.

Philippines.—Projects include supplies and equipment for two laboratories—one for the production of BCG vaccine and the other for the diagnosis of tuberculosis. Supplies for a rural health programme with special emphasis on maternity and child welfare are also included.

Thailand.—Supplies and personnel are to be provided for a combined programme to fight both yaws and venereal disease. A maternal and child health programme including dental hygiene is also under consideration.

Similar programmes in other areas in Asia are also under consideration, and may be expected to be finalized shortly. Mr. Pate and his party consisting of Mr. Myron Schmittlinger of UNICEF, New York Headquarters, Mr. S. M. Keeny, UNICEF Director for the Far East, and Dr. Cottrell, W.H.O. Adviser to UNICEF Far East Headquarters, are leaving India to-morrow for Pakistan where they will discuss programmes for meeting the needs of that country's mothers and children. Messrs. Pate and Schmittlinger have already completed a world tour including Australia, New Zealand, Indonesia, Singapore, Thailand and Burma.

The officers of both UNICEF and W.H.O. are confident that the pattern thus established between their organizations for pooling international resources in money and expert knowledge represents an important forward step in improving the health of mothers and children, and thus strengthening future generations of people in the many parts of the world where they are co-operating.

IV. W.H.O. ANTIBIOTICS PROGRAMME DRAFTED BY EXPERTS: RECOMMENDATIONS TO THIRD WORLD HEALTH ASSEMBLY (SEA/PR/50-26, dated 3rd May, 1950)

A world programme designed to stimulate research in the field of antibiotics, and to improve the available production and distribution of this new group of

powerful drugs, has been drafted by the W.H.O. Expert Committee on Antibiotics which held its first session in Geneva last month. The experts met under the chairmanship of Dr. Ernst B. Chain, F.R.S., of the Health Institute, Rome, Italy, co-discoverer of the uses of penicillin, and included Dr. Selman A. Waksman (U.S.A.), discoverer of streptomycin, and leading scientists from France, Great Britain and Sweden, Dr. S. S. Sokhey, late Director of the Haffkine Institute, Bombay, and now Assistant Director-General of W.H.O., was also present at the meetings of the Expert Committee.

The more important antibiotics include penicillin, streptomycin, chloromycetin, aureomycin, tyrothricin and basitracin. Other recently discovered antibiotics, whose potentialities are not yet determined, are nisin, neomycin, terramycin, subtilin and esperin.

As regards the present position in antibiotics work, the experts underlined that 'such rapid changes occur in this field that every effort should be made at training scientists and technologists to be able to keep abreast of new developments'.

The best way to increase the potential of antibiotics production, the experts suggested, was to develop training facilities for the highly-skilled personnel needed and to stimulate basic research in this expanding and very promising field of science. The World Health Organization could best assist, in their opinion, by sponsoring research programmes and granting long-term research fellowships.

The Expert Committee recommended that W.H.O. make every effort to procure equipment and supplies for national governments wishing to develop their own antibiotics production and unanimously declared that Podbielnak extractors, considered essential for the economic production of penicillin, could not in the present state of knowledge be used for processes connected with biological warfare.

The experts were also of the opinion that W.H.O. should organize controlled investigations into the therapeutic effects of the new drugs which have taken a prominent place in the treatment of infectious diseases of men and animals.

The report of the W.H.O. Expert Committee is being submitted to the 'Ad hoc' Committee of the W.H.O. Executive Board, now meeting in Geneva, prior to the opening of the Third World Health Assembly on 8th May.

V. THIRD WORLD HEALTH ASSEMBLY TO OPEN ON 8TH MAY

(SEA/PR/50-27, dated 3rd May, 1950)

THE World Health Assembly, supreme body of the World Health Organization, is to meet for the third time on 8th May, 1950, in the Palais des Nations, Geneva, Switzerland. Health Ministers and top-ranking health officials are expected to attend from a large number of the 68 countries which have ratified W.H.O.'s Constitution. Delegates anticipate that the Agenda, which contains 59 main items covering the policies, finances and present and future programmes of W.H.O., will not be exhausted before the end of May.

The two previous World Health Assemblies were held respectively in Rome (1949) and Geneva (1948).

The Assembly will consider requests for admission to W.H.O. membership from four countries: Indonesia, Viet-Nam, Cambodia and Laos.

Following discussions last September at a meeting of the W.H.O. Regional Committee for South-East Asia, the Ceylon Government is proposing that the South-East Asia Region should have fuller representation on the W.H.O. Executive Board. At present only one of

the 18 members of the Board is nominated by a South-East Asian country. He is the Board's Chairman, Sir A. Lakshmanaswamy Mudaliar, Vice-Chancellor of Madras University.

On the Agenda of the Committee on Administration, Finance and Legal Matters, which, with the Committee on Programme is expected to shoulder the bulk of the Assembly's work, is the question of arrears in the payment of member countries' contributions to W.H.O. for 1948, 1949 and 1950. As of 15th April, 1950, only 84 per cent had been paid of the total contributions due to W.H.O. for 1948, 79 per cent for 1949, and 12½ per cent for the current year. The Committee will consider whether or not to maintain the provisional cut of 1,200,000 dollars made by the Executive Board in the 1950 budget (originally \$7,500,000), and will discuss the regular budget estimates of \$7,600,000 for 1951.

This Committee will also consider the intimations received from seven States that they no longer consider themselves members of W.H.O., and the attitude to be adopted by the Assembly in view of the fact that the W.H.O. Constitution makes no provision for withdrawal. The seven countries are Albania, Bulgaria, Byelorussian S.S.R., Czechoslovakia, Romania, Ukrainian S.S.R., and U.S.S.R.

The principal task of the Committee on Programme, will be to consider and approve proposals for the 1951 Programme of W.H.O. as submitted to the Assembly by the W.H.O. Executive Board. The proposed programme, which is contained in a 280-page printed document, will be dealt with under three main heads:—

- (1) *Central technical services*, representing functions inherited by W.H.O. from previous organizations, and long recognized as essential to international health work. These include services in International Epidemiology and Quarantine, Health Statistics, and the Co-ordination of Research;
- (2) *Communicable diseases*, of which there are over thirty on W.H.O.'s action list; and
- (3) *Advisory services* of direct assistance to Member Governments in strengthening health administrations and guiding the expansion of public health services.

The Committee's Agenda includes consideration of reports from more than twenty W.H.O. Expert Committees and Groups on different aspects of W.H.O.'s programme.

A four-year plan of work to start in 1952, which was drawn up by the W.H.O. Executive Board in January, will also be submitted to the Programme Committee. Considered of far-reaching importance, the four-year plan includes proposals for a broad regionalization of the Organization's work with thorough decentralization of functions.

India's delegation to the Third Health Assembly will be led by the Minister of Health, Rajkumari Amrit Kaur, the value of whose practical and constructive contributions to discussions in previous World Health Assemblies has been generally recognized. She will be accompanied by Dr. K. C. K. E. Raja, Director-General of Health Services, Dr. C. K. Lakshmanan, Director of the All-India Institute of Hygiene and Public Health, Calcutta, and Dr. C. V. Ramchandani, Assistant Director-General of Health. Dr. Raja was a member of the W.H.O. Expert Committee on Epidemiology and Quarantine which met last December, while in February Dr. Lakshmanan attended the first meeting of the W.H.O. Expert Committee on Professional and Technical Education.

Sir A. Lakshmanaswamy Mudaliar will also attend the Assembly in his capacity of Chairman of the W.H.O. Executive Board.

The leader of Ceylon's delegation will be The Hon'ble S. W. R. D. of Health. Assisting him will be ... Williams, Assistant

Director of Sanitary Services and Dr. W. A. Karunaratne, Medical Officer of Health.

VI. THIRD WORLD HEALTH ASSEMBLY OPENS IN GENEVA: W.H.O. DIRECTOR-GENERAL'S APPEAL FOR NATIONAL INVESTMENT IN HEALTH

(SEA/PR/50-28, dated 8th May, 1950)

THE Third World Health Assembly opened in Geneva this morning in the presence of important delegations from most of the sixty-nine Member States of the World Health Organization. At the opening session the delegates heard speeches from Dr. Karl Evang (Norway) who was President of last year's Assembly in Rome, from Mr. Trygve Lie, Secretary-General of the United Nations, and a welcoming address from Dr. Brock Chisholm, Director-General of W.H.O.

'We must do all we can to convince governments that at a time when they are allotting millions for unproductive rearmament purposes, at least a few more millions should be invested in the most precious values they have to protect: the health of their peoples and their peoples' children', said Dr. Chisholm in an earnest appeal to governments to appreciate the significance of health in the promotion of human prosperity and to support with adequate financial means the various national and international efforts to improve the status of world health. Dr. Chisholm continued 'If recent history has taught us a lesson, it is surely that peace and security are dangerous illusions when the majority of people on earth are sick and hungry'.

Welcoming the delegates to the Assembly, Dr. Chisholm said: 'Within the limitations we have had to face during 1949, a serious effort has been made to implement the decisions of the First World Health Assembly. Under the direction of the W.H.O. Executive Board, the W.H.O. Secretariat has now been established on a basis which should ensure a maximum degree of efficiency with enough flexibility to provide modifications which may prove necessary in the light of experience.

'Thanks to the generous help of the Swiss authorities and the co-operation of the United Nations', Dr. Chisholm continued, 'we shall soon have a permanent headquarters in the "Palais des Nations" here in Geneva'.

After reviewing W.H.O. activities since the inception of the organization, Dr. Chisholm went on: 'We cannot congratulate ourselves on a job well done. Quite the contrary. We are still far from the paramount objective defined in the W.H.O. Constitution as "The attainment by all peoples of the highest possible level of health". What is lacking and what is urgently needed is a greater determination on the part of National Administrations to expand the health resources of their countries, thus raising the health standards of their populations, seconded by an active international effort to ensure the widest possible application of the discoveries which have been made in the fields of medical science and public health techniques.'

To ensure sufficient funds for W.H.O.'s work primarily at the national level, affirmed Dr. Chisholm, was one of the major responsibilities they must squarely face. The governments of the world must have the courage to recognize these facts and to accept the responsibility they impose.

'The simple truth which must unite us', Dr. Chisholm declared, 'is that world health, world security and world peace are indivisible and closely related. The tension between the great powers and others is not only a threat to peace but also the most serious obstacle to economic and social progress. All governments must do their utmost to end this state of tension

which is increasingly dividing the world. We must go back to the principles of the United Nations Charter which until now have never been applied, although their application is now more necessary even than when they were formulated in 1945.

'The time has come', concluded the Director-General, 'when governments instead of wasting their energies in political quarrels should devote them to realizing the aim of the United Nations which is to build a healthy, prosperous and peaceful world'.

To-morrow (Tuesday) at noon, Mr. Trygve Lie is to lay the foundation stone of the new wing of the Geneva Palais des Nations which is to house W.H.O. A number of Swiss notables will be present at the ceremony.

Background note.—The Palais des Nations, built on the shores of the Lake of Geneva for the old League of Nations, has been an active centre of international affairs since 1936. It became the property of United Nations in 1946 and now houses a number of U.N. bodies, including W.H.O.

To provide adequate accommodation for the expanding Headquarter of W.H.O., the Swiss Government has contributed three-quarters of the cost of building a new wing to the Palais and making certain internal changes which are expected to provide about 210 additional offices.

WORK OF LEPER MISSION IN INDIA

(From Release No. B.F. 548 issued by British Information Services, Office of the U. K. High Commissioner for India, New Delhi)

THE increasing work in India of the Mission to Lepers is described in its 75th annual report just published by the organization's Council in London.

The Faizabad (U. P.) Home of the Mission reports great progress in co-operative work for patients, particularly farm work which apart from its therapeutic value helps to break down class barriers. In many centres, says the Mission's report, patients and staff work together, helping to sink wells, instal pumps and in some cases assisting in the medical work itself for which they receive training from the medical staff.

The report also says that several new projects have been undertaken, many of them specially planned for child patients. With a view to increasing the number of Indian doctors on its staff, the Mission has awarded scholarships to three Indian medical students.

The work of the Mission at Raniganj, and at Tarn Taran (Punjab), has been considerably hampered by overcrowding. The activities of these centres, according to the report, have only been maintained with the help of emergency grants from the Mission, in addition to ordinary grants.

DRUGS RULES, 1945

AMENDMENT OF SCHEDULE C(1)

(No. F.1-7/48-D., Government of India, Ministry of Health, New Delhi, the 16th May, 1950)

NOTIFICATION

IN exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely:—

In Schedule C(1) to the said Rules, for items 1, 3, 5, 6 and 7, the following items shall respectively be substituted, namely:—

- '1. Drugs belonging to the Digitalis group and the preparations thereof not in a form to be administered parenterally';
- '3. Adrenaline and the preparations thereof not in a form to be administered parenterally';
- '5. Vitamins and the preparations thereof not in a form to be administered parenterally';
- '6. Liver extract and the preparations thereof not in a form to be administered parenterally'; and
- '7. Hormones and the preparations thereof not in a form to be administered parenterally.'

(Sd.) J. N. SAKSENA,

Under Secretary.

DRUGS ACT, 1940

(Notification No. F.1-42/47-D., Government of India, Ministry of Health, dated New Delhi, the 27th May, 1950)

IN exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely:—

In Schedule F annexed to the said Rules, in Part XII, under the heading 'D-Preparations containing any vitamins in a form not to be administered parenterally', in the sub-head relating to 'Labelling' for entry 1, the following entry shall be substituted, namely:—

- '1. The number of units and/or the actual weight of each vitamin per unit volume and/or weight shall be declared on the label.'

(Sd.) J. N. SAKSENA,

Under Secretary.

TWENTY-THREE INDIAN DOCTORS TO ATTEND CONGRESS OF RADIOLOGY

INTERNATIONAL GATHERING IN LONDON

(Reproduced from Release No. B.F. 734, issued by British Information Services, Mansing Road, New Delhi)

DOCTORS from all over the world, including India, will meet in Britain next month for the Sixth International Congress of Radiology, to be held in London from 23rd to 29th July.

Thirty-nine countries are sending official delegations, each of which will consist of five persons, but a large proportion of the attendance will be radiologists from overseas countries belonging to radiological societies who will come quite independently.

India will be well represented by independent delegates as well as her official delegation. The latter will consist of Dr. K. P. Mody (Chairman) from Bombay, Dr. M. D. Joshi (Bombay), Captain M. Mukherjee (Calcutta), Dr. P. Rama Rao (Madras) and Dr. S. C. Sen (New Delhi). In addition, 18 other doctors from India are expected to attend.

Before the war these congresses were held triennially and were regarded as a valuable forum for the exchange of scientific ideas. The first took place in London in 1925 and was followed by congresses in various large cities in Europe and once in the U.S.A. British radiologists are proud to act as hosts on this forthcoming occasion as it will be the silver jubilee of these meetings.

A major feature of the London congress will be a technical exhibition of apparatus—the largest of its

kind ever held—which will include the products of some 70 exhibitors from nine countries. Every phase of x-ray technology will be dealt with—from high voltage therapy apparatus to dark-room accessories. There will be all kinds of equipment for branches of physiotherapy, such as short-wave radiation therapy. In addition to medical equipment, manufacturers will exhibit material for use in industrial radiography.

There will also be a scientific exhibition to demonstrate the recent advances in the art and science of radiology over a wide field. This will be in four main sections: history (in collaboration with the Science Museum); radio-diagnosis; radio-therapy; physics and biology.

Running concurrently with the Congress will be a series of demonstrations of radiological interest at famous London hospitals.

The Indian Medical Gazette Fifty Years Ago

TUBERCULOSIS IN INDIA

(From the *Indian Medical Gazette*, June 1900,
Vol. 35, p. 222)

THE prevalence of tuberculous diseases in India is a subject which has been several times discussed in these columns, and in the new volume of the Report of the Sanitary Commissioner with the Government of India (for 1898), Dr. A. Crombie contributes an interesting note in the form of a report to the India office of his delegation to attend the Tuberculosis Congress in Berlin in May 1899. Dr. Crombie commences by briefly summarizing the conclusions of the Congress as to the essential nature of the disease, and the questions of ætiology and heredity. These points were dealt with in our columns at the time of the Congress; at present we propose only to refer to the question of the prevalence of the disease in India. When we use the word 'Tuberculosis' in its broad sense implying all forms of local tuberculous disease, we agree with Dr. Crombie in saying that 'they take quite a subordinate place in the sickness and mortality of India', but on the other hand, tubercle of the lung or phthisis is certainly almost as common in many parts of India as it is in England. Certainly we believe most of our readers will agree that 'scrofulous' or 'strumous' diseases of the glands and joints are much less common in our Indian hospitals than in any European one. Chevers stated that he never even saw a case in India. Dr. Crombie quotes Webb, Waring, and Birch as agreeing that scrofula is very rare in India. *Tuberculosis mesenterica* is apparently also rare in India, but in the case of children we may remember that it is practically impossible to obtain autopsies, and the case would probably be returned as 'chronic diarrhoea'. Cases do certainly occur among European children in

India, but nothing like to the same extent as in Europe. Tuberculous peritonitis is, in our experience, by no means uncommon in India; we have seen cases both in sepoys and in prisoners. Dr. Crombie notes that he never saw a case of tuberculous disease of the hip joint in India, and Birch, with his vast experience at the Medical College, Calcutta, agrees with this opinion.

On the other hand, tuberculous disease of the lungs is far from uncommon in many parts of India, perhaps it is more so in the damper parts than in the drier regions. That phthisis is common among Gurkhas and among Burmans is well known. The statistics of troops are somewhat misleading upon this point; the figures show that the rate of admission among sepoys for tubercle of the lungs is only 2.5, but it must be remembered that these are picked men in the prime of life. In jails, on the other hand, the death-rate fairly represents the adult male population of the province, and among them we find an admission rate of about 7 per mille, and a death-rate of about 3 per mille. Dr. Crombie is apparently inclined to think that the ratio of tubercle of the lungs has increased of late years in jails, but on this point, from an examination of the *post-mortem* records of several large Central Jails in Bengal, we are of opinion that it is only more accurate diagnosis which is responsible for the apparent increase. Let any one who doubts this read through the *post-mortem* records and he will find numerous cases returned as deaths from 'chronic diarrhoea' or 'chronic dysentery', in which there is noted plain evidence of advanced tuberculous disease of the lungs. Then again Goodeve and Moore years ago pointed out how apt tubercle of the lungs is to run a latent course in the native. The patient will perhaps complain only of diarrhoea, or weakness, or fever, or less often of cough. Unless the lungs are examined the diagnosis may not be made till the body is on the *post-mortem* table. In public dispensaries over and over again it will be found that a man is treated for 'cough' or 'fever' or such symptom when he is really suffering from tubercle of the lungs. So far from phthisis having increased of late years in the jails of India, we believe it is on the decrease rather, and that cases are more carefully diagnosed and examined than they used to be.

Dr. Crombie can find no law indicative of the influence of climate on the prevalence of phthisis. The figures from year to year are too contradictory to be of any use in this connection. The question of racial immunity is also a difficult one. As regards India, it would appear that Dogras and Gurkhas suffer most, Rajputs and Sikhs least, but as these figures refer only to picked men in the prime of life in regiments, they are of not much value in attempting to settle this question. For our own parts, we think the damper, moister climates of India produce the

most cases of tubercle, while in the case of hill tribes, their known liability may be to a great extent due to their habit of living for sake of warmth and comfort in close, small, ill-ventilated houses, which also explains the high death-rate from consumption in Russia and Austria. While, therefore, we maintain that tubercle of the lungs is by no means an uncommon disease in India, we agree with Dr. Crombie that tuberculosis, as a whole, is certainly prevalent to a lesser degree than in Europe, and the causes of this lesser prevalence as given by Dr. Crombie will be accepted by all. These are briefly as follows :—

(1) The comparative infrequency of bovine tuberculosis in India. It is not unknown, but is certainly rare, though it will never be fully known to what extent Indian cattle are subject to this disease, till the tuberculin test has been more largely made use of. (2) The Indian habit of boiling the milk certainly must prevent much tuberculosis being spread by milk and explains the immunity of native children from *tabes mesenterica*. (3) Beef is little used, and stall-fed oxen are unknown in India. (4) The flesh of the goat is much used, and it is an animal refractory to tuberculosis. (5) Dr. Crombie also mentions the open-air occupations of the natives. This is chiefly applicable to the rural population, nor do the natives of India

universally use mat or reed huts; millions in the N.-W. Provinces and Punjab inhabit close, small, ill-ventilated houses with thick mud walls, they however sleep in verandahs or in the open air at night for most months of the year. (6) Dr. Crombie also mentions his abstinence from alcohol as being in favour of the native of India. (7) The use of *ghi* instead of butter would have some effect in a like direction. Again much of the immunity of native children is due to the infrequency of diseases predisposing to tubercle, as whooping cough and scarlet fever. Measles is not rare in India, but it is almost invariably mild, a fact which contrasts strongly with the extreme mortality which has been attributed to measles in Egypt, where it is the most fatal disease in childhood.

We have only touched upon some of the interesting points raised in Dr. Crombie's report; for our own part, when we remember the well-known reluctance with which the native of India admits fresh air and light into his house, we wonder not that phthisis is not unknown, but that it is not more prevalent. Part of the explanation apparently is that in Dr. Crombie's words the 'Native of India appears to have instinctively adopted all the dietetic habits best calculated to protect him against bovine tuberculosis'.

Current Topics, Etc.

Chloramphenicol in Treatment of Infantile Gastro-Enteritis

By K. B. ROGERS AND OTHERS

(Abstracted from the *British Medical Journal*, ii, 31st December, 1949, p. 1501)

IN Birmingham, as in many other parts of Great Britain where it is sought, *Bact. coli* B.G.T. has been found to be intimately associated with epidemic infantile gastro-enteritis. The enteritis did not respond to the administration of sulphonamides, penicillin or streptomycin, but the response, both clinically and bacteriologically, to chloramphenicol has been most encouraging.

Treatment of Pulmonary Tuberculosis with Para-Aminosalicylic Acid and Streptomycin

(From the *British Medical Journal*, ii, 31st December, 1949, p. 1521)

A CLINICAL trial of *p*-aminosalicylic acid (PAS) and streptomycin in pulmonary tuberculosis was undertaken in 1948 by the Medical Research Council, with the co-operation of the British Tuberculosis Association. The trial is not yet completed, but certain results already obtained are of such importance that the joint

committee responsible for guiding the trial has decided to issue the following preliminary statement.

A major disadvantage in the use of streptomycin is that the period of effective therapy is limited in many patients by the emergence of streptomycin-resistant strains of tubercle bacilli after five or more weeks of treatment. It has been thought by many workers that the addition of another tuberculostatic agent might be sufficient to suppress the resistant strains, which in the initial phases are present in very small numbers; published reports on a few cases treated with PAS and streptomycin have been encouraging. The present investigation was planned to examine, by the method of controlled trial, the possibility that PAS has this property, and at the same time to assess the clinical effect of this drug alone and in combination with streptomycin. Accordingly, three treatment groups of over 50 cases each were observed: (a) PAS alone (20 g. of the sodium salt daily); (b) streptomycin alone (1 g. daily) and (c) both drugs together (20 g. of the sodium salt of PAS and 1 g. of streptomycin daily). The methods were similar to those employed in the first M.R.C. clinical trial of streptomycin in pulmonary tuberculosis (*British Medical Journal*, ii, 1948, 769), and the type of case was again defined as follows: acute rapidly progressive bilateral pulmonary tuberculosis of recent development, unsuitable for collapse therapy, in young adults aged 15 to 30. After acceptance for the trial by a panel, patients were allocated to one of the three treatment groups by a method of random selection. The prescribed treatment was given for three months in each case. Clinicians and pathologists at eleven hospital centres have co-operated in this investigation, keeping uniform records, employing

standard clinical and bacteriological procedures, and reporting results at regular intervals to the Council's Tuberculosis Research Unit, where the grouped results have been analysed.

For this well-defined type of case of pulmonary tuberculosis the trial has demonstrated unequivocally that the combination of PAS with streptomycin reduces considerably the risk of development of streptomycin-resistant strains of tubercle bacilli during the six months following the start of treatment. The conclusion is applicable so far only to the acute form of disease treated, and it remains to be seen whether the same results are obtainable in other forms of tuberculosis amenable to streptomycin therapy. Furthermore, the conclusion is appreciable only to the large dose of PAS used; this dose causes discomfort in some patients, and it has been agreed to find out, by further trials, whether smaller doses would achieve the same result. It must be stressed also that streptomycin is effective only in certain forms of tuberculosis, and the finding reported here must not be interpreted as indicating that a combination with another drug will be effective in those forms in which little result would be expected from streptomycin alone.

Treatment of a Lung Abscess by Inhalation of Micropulverized Penicillin

By D. T. O'DRISCOLL

(Abstracted from the *Lancet*, ii, 19th November, 1949, p. 945)

A LUNG abscess complicating lobar pneumonia, in a patient with auricular fibrillation, was treated with micropulverized penicillin delivered through an arohaler.

This method of treatment proved remarkably effective and saved the patient from a surgical operation.

The administration of antibiotics in the form of a fine powder, by means of suitable inhaler, might be equally successful in other conditions with lung cavitation, in which systemic administration does not bring the antibiotic into contact with the organisms in a therapeutic concentration.

Hyaluronidase in Pediatrics

(From the *Lancet*, ii, 17th September, 1949, p. 522)

HYALURONIDASE, a mucolytic enzyme obtained from many sources, including mammalian testes and semen, has been found to promote the absorption of fluid injected intramuscularly or subcutaneously; it also accelerates the absorption of penicillin, streptomycin, adrenaline, and procaine. The benefit of using this enzyme is perhaps most evident in the treatment of children, where intravenous therapy is often fraught with difficulty; and in this issue Professor Gaisford and Dr. Evans show that dehydration in children responds as well to saline administered subcutaneously with hyaluronidase as to intravenous infusions, although the response is rather less rapid.

Schwartzman reports that of 158 children only one was allergic to hyaluronidase in the purest form available. In his experience the optimal dose for parenteral infusions is 80 μ g. per area per dose, and any increase beyond this amount does not further hasten absorption. Like Gaisford and Evans, he finds that plasma is absorbed when given subcutaneously with the enzyme; but in an infant with serious diarrhoea and an initial serum-protein level of 4.7 g. per 100 ml., absorption took place only after the protein level had been raised

by a preliminary intravenous infusion. In anæmic children who received subcutaneous injections of whole blood with hyaluronidase, absorption was confirmed by repeated haemoglobin estimations.

If the potential value of hyaluronidase is to be exploited, a standard and highly purified preparation will be needed. The material can be easily prepared from bovine serum, which may be had in fairly large quantities. The potency of the enzyme is easily tested.

Low-Salt Diet in Treatment of Hypertension and Hypertensive Heart Disease

By H. O. BANG *et al.*

(Abstracted from the *British Medical Journal*, ii, 26th November, 1949, p. 1203)

TWENTY-SIX patients with hypertension, in some associated with heart failure and/or nephropathy, were treated with a diet containing 1 g. of sodium chloride. Sixteen of these patients had a fall in the blood pressure, which rose to some extent again after a daily addition of 4.5 g. of sodium chloride. In addition, the low-salt diet proved to have a favourable effect on cardiac oedema. Owing to the continuous loss of sodium the treatment is contra-indicated in certain cases of chronic nephritis.

Remissions in Arthritis

(From the *Journal of the American Medical Association*, Vol. 141, 12th November, 1949, p. 782)

REMISSIONS in arthritis may occur after the use of a variety of therapeutic agents, such as gold therapy, hyperthermia with typhoid vaccine, massive doses of activated ergosterol, bismuth therapy, administration of cinchophen or foreign protein and bee venom therapy. Hench re-emphasized what had been noted by several earlier observers, notably by Still and by Wishart, that hepatic damage with, and occasionally without, jaundice is decidedly beneficial to patients with arthritis. He stated that the future outlook for patients with chronic arthritis is decidedly hopeful and that within the body of patients who have even the severest arthritis powerful corrective forces lie dormant which merely await the proper stimulation. Archer in a more recent publication advances the hypothesis that a potent denominator for remissions in cases of arthritis is present when the patient becomes pregnant or jaundice develops and that the denominator is hepatic damage and/or a dysfunction. The same hypothesis, in his opinion, would explain the remissions observed in patients with arthritis after the use of gold salts, cinchophen, bismuth compounds, fever therapy, viosterol in massive doses and other hepatotoxic drugs. He mentions six biochemical factors present in pregnancy which operate also in hepatocellular and extrahepatic obstructive jaundice. These biochemical changes, for the most part, are the result of hepatic damage and dysfunction, and the common biochemical denominators, singly or in combination, may possess antirheumatic properties. Archer describes a method of approach which consists of the simultaneous administration of gold salts and large doses of viosterol to produce a mild toxic hepatitis, the administration of these agents being carefully controlled by serial tests of hepatic and renal function. Hench, Kendall, Slocumb and Polley reasoned that the antirheumatic substance X might be an adrenal hormone. The result of this reasoning is the discovery of the

adrenal cortex hormone called compound E and of the adrenocorticotrophic hormone.

[For compound E the possibility of its manufacture from plants see Editorial, *I.M.G.*, April 1950, page 159.—Editor, *I.M.G.*]

Amoebiasis in Infancy

By P. C. C. DE SILVA

(Abstracted from the *British Medical Journal*, ii, 26th November, 1949, p. 1208)

AMOEBIAC dysentery, acute or chronic, is said to be uncommon in infancy. Manson-Bahr states that, below the age of 10, 0.9 per cent of dysenteries in European children are amoebic. He adds that in native children amoebic dysentery is probably not uncommon. Izar held that even infant at the breast were not immune. Musser stated that amoebiasis was a disease of adult life rarely contracted before the age of 10. Karunaratne gave the incidence of amoebic hepatitis in children under 5 as varying from 7.9 per cent to 35 per cent in different series. Howell and Knoll found rates of 3.1 per cent and 4.8 per cent in two separate series of children in the United States. In Cairo, Perry and Bensted found *Entamoeba histolytica* in 13.9 per cent of children with dysentery, and Willets discovered this organism in 25 per cent of Filipino children. Craig stated that the rarity of amoebiasis in children was not due to any inherent insusceptibility to infection but to their much-reduced chance of contracting the disease. This statement is not applicable to infant life in Ceylon.

Forty cases of pathologically proved *E. histolytica* infection in infants in Colombo and its environs are presented. Of 291 cases of infantile diarrhoea in children under 2 years of age, 15.9 per cent were infected with *E. histolytica*. Fourteen cases were 1 year of age and 26 between 1 and 2 years. Twenty-nine of the cases were infected with *E. histolytica minuta* and the others with the larger type. Half the cases were of the acute and half of the chronic and relapsing variety. Treatment given was by emetine parenterally and carbarsone orally. Of the cases followed up, 80 per cent indicated satisfactory results.

Deoxycortone Acetate and Ascorbic Acid in the Treatment of Rheumatoid Arthritis

By D. L. VAY

and

G. E. LOXTON

(Abstracted from the *Lancet*, ii, 17th December, 1949, p. 1134)

LEWIN and Wassén report that the combined injection of deoxycortone acetate and ascorbic acid caused temporary improvement in cases of rheumatoid arthritis. Our object here is simply to state that we have been able to confirm these results in a considerable proportion of cases. Further work is proceeding on the mode of action of these substances and the physiological changes they produce and will be reported in due course. We have studied 23 cases, using the recommended dosage of 5 mg. of deoxycortone intramuscularly, followed within five minutes by 1 g. of ascorbic acid given intravenously.

The natural history of rheumatoid arthritis has not been fully studied owing to the practical difficulty of following cases over the long and variable course of the disease without giving any treatment. The general view, however, is that 25 per cent of cases undergo spontaneous recovery, 50 per cent improve, and 25 per cent deteriorate despite treatment. To prove beyond any possible doubt the value of a

treatment, it is necessary to watch a long series of cases over a period with careful controls and to establish a significantly better improvement rate in the treated cases. But in our experience, and we believe the experience is general, although the disease may have a comparatively sudden onset, it never undergoes such a sudden improvement as we have witnessed, in some cases within a few hours or even minutes of injection of deoxycortone and ascorbic acid.

Twenty-three cases of polyarthritis, mostly instances of rheumatoid arthritis, have been treated with deoxycortone acetate and ascorbic acid injections. Six of these exhibited rapid striking improvement lasting several hours, 15 were temporarily improved, and 2 failed to respond. We regard these findings as substantiating the claims of Lewin and Wassén that these substances given in conjunction exert a beneficial action in some cases of rheumatoid arthritis.

Chloromycetin in Scrub-Typhus

By H. McC. GILES AND OTHER

(Abstracted from the *Lancet*, i, 7th January, 1950, p. 16)

SIXTEEN cases of scrub-typhus in British, Gurkha, and Chinese soldiers in Malaya are reported.

Each patient was given one dose of 3 gr. of synthetic chloromycetin; fifteen responded fully and required no further treatment.

One patient did not improve within 10 hours, and was given an additional 2.25 g. of chloromycetin, after which he made a rapid recovery.

In the light of these results it is suggested that the routine treatment of scrub-typhus need consist of no more than a single dose of 3 g. of chloromycetin. If, however, obvious improvement is not apparent within 10.12 hours, an additional dose of 1 g. should be given, followed by 0.25 g. 3-hourly to a total of about 6 g.

An Unusual Case of Shoplifting

(From the *Lancet*, ii, 17th December, 1949, p. 1158)

ON 2nd December, a 24-year old woman, who admitted having stolen goods to the value of £4 15s. from three London stores, was fined £10 with 5 guineas costs at Great Marlborough Street police-court. On the day in question she had, according to her story, taken some 20-25 mg. of amphetamine sulphate, and a medical witness testified: 'In my opinion, if this girl took the number of tablets she claims to have taken, they would induce hilarity and irresponsibility; and she certainly would not realize the effect of what she was doing'. Imposing the fine, the magistrate observed: 'I would not accept that from you or any body else. I can see absolutely no connection between the tablets and a girl going from store to store plundering shopkeepers.'

The accused woman, who was reported to be of excellent character, had consulted her doctor on 21st November because of varicose veins; and, since she was over-weight, he prescribed 5 mg. amphetamine sulphate ('Benzedrine') three times daily with the object of reducing her appetite. On 22nd and 23rd November she took the prescribed doses, and she was said to have behaved excitably and to have remarked that the medicine made her feel 'very, very happy'. On 24th November, she apparently took a 5-mg. tablet on rising, 2 further tablets at 10-30 a.m. and either 1 or 2 more (she could not remember which) at 12 noon; for breakfast she had one slice of toast, and she ate no lunch. In the early afternoon she remarked that she felt as if she were 'floating on air'. At

4-15 p.m. she was arrested by a woman detective officer, who said that the woman behaved in a very extraordinary way which was compatible with her being under the influence of some drug. On being told that she would be arrested, she laughed heartily and remarked: 'Yes, I took them; but it's all a game. It's such fun'.

War-time tests of the analeptics, amphetamine and methedrine, showed that a dose of 15 mg. sometimes evokes irresponsible and irrational behaviour, with euphoria, confusion, and excitement. The reaction which varies between one person and another and in the same person from one occasion to another is unpredictable from the individual's normal personality.

Protracted Nervous Complications of Typhoid Fever

By G. H. JENNINGS

(Abstracted from the *Lancet*, ii, 31st December, 1949, p. 1218)

A case of typhoid myelitis and neuritis of very protracted course is described.

The nervous symptoms came on at the end of the fifth week of a moderately severe attack of typhoid fever and resembled encephalitis; signs of neuritis and of a lesion of the spinal cord followed some weeks later.

Recovery, though very slow, has been continuous, but even after 5½ years is not yet quite complete.

The long period of healing suggests that there are permanent changes in the spinal cord, but, judged by present signs, these changes are surprisingly slight.

The progressive improvement seems to have been due to the recovery of demyelinated tracts, including the pyramidal, and to the clearing of an associated neuritis.

Treatment of Leprosy with Diamino-Diphenyl Sulphone by Mouth

By J. LOWE

(Abstracted from the *Lancet*, i, 28th January, 1950, p. 145)

DIAMINO-DIPHENYL sulphone (D.A.D.P.S.) was the first sulphone synthesized, but its pharmacology and therapeutic effects were not studied until 1937, when Buttle *et al.* found that it possessed remarkable properties. In streptococcal infections in mice, doses of 4.0 mg. were as effective as doses of sulphanilamide a hundred times greater. Its acute toxicity was however ten to twenty times greater than that of sulphanilamide.

When Rist *et al.* demonstrated the action of sulphone in experimental tuberculosis in animals, D.A.D.P.S., 'Promin' and 'Diasone' were used in the extensive animal experiments which followed; D.A.D.P.S. showed up well, producing some results comparable to those of other sulphone in higher doses.

In the trials of sulphone in human tuberculosis, because of its reputed toxicity to man, no attempt seems to have been made to use D.A.D.P.S., possibly the most potent sulphone. The results of sulphone treatment in human tuberculosis have been disappointing.

Workers in the United States have reported that the results of sulphone treatment in leprosy is much superior to those of any previous form of treatment, though it has limitations. Workers in other countries are now reporting similarly.

Practically all this work has been done with the relatively expensive and complex proprietary sulphones, puomin, diasone, and lately 'Sulphetrone'. Until recently no attempt was made, once more because of its reputed toxicity, to use the simpler and cheaper D.A.D.P.S. Cochrane reports an attempt to use D.A.D.P.S. in leprosy, giving twice-weekly injections of 125 g. but he has found that toxic effects are too common and too serious to make this treatment widely applicable, though the results were good.

The question which this paper attempts to answer is: can it be used in treating human leprosy with safety and with good therapeutic effect?

The special properties of D.A.D.P.S. are outlined. *In vitro* and in animals its antibacterial power is possibly the greatest of any of the sulphones.

The accepted idea that D.A.D.P.S. is too toxic for use in human beings is examined and found to be erroneous.

A régime of oral administration of small doses, rising very slowly from 100 mg. a day to the standard 300 mg. a day in 5 weeks, is recommended, treatment being continuous. This régime does not produce toxic effects of any consequence, and it will maintain a blood level of about 1 mg. per 100 ml., which on theoretical grounds should be a therapeutic level in leprosy.

The almost complete absorption from the gut and slow elimination by the kidney explain the relatively high blood-levels attained with such small doses, and also explain the toxic effects reported with the much higher doses used by others.

In the avoidance of toxic effects, very slow induction of D.A.D.P.S. treatment is of paramount importance.

A therapeutic trial of this treatment in 88 patients with leprosy for periods up to a year is described.

Of the fifty lepromatous cases treated for more than 6 months, none show deterioration; 72 per cent show clinical improvement; 62 per cent show bacteriological improvement; and three have become bacteriologically negative. These results compare very favourably with those seen here with complex proprietary sulphones. There are indications that D.A.D.P.S. is acting more rapidly than these other sulphones.

In fifteen 'tuberculoid' cases treated for 4-10 months the response has been apparent within a month, and sometimes within a fortnight or less, with complete subsidence of activity of the skin lesions within six months; the nerve involvement however takes longer to subside. The results, though similar to, appear to be more rapid than those seen with other sulphones in similar cases.

The cost of D.A.D.P.S. for the treatment for one patient for a year on this basis is 14s. The cost of treatment with the complex proprietary sulphones is about twenty times as much.

A régime for twice-weekly administration of D.A.D.P.S. by mouth suitable for outpatients is outlined, the cost being 7s. a year per patient. Injections seem to be unnecessary.

It is suggested that the more complex sulphones act by being hydrolysed to D.A.D.P.S. in the body. They are incompletely absorbed from the gut and incompletely hydrolysed to D.A.D.P.S. They thus provide an unnecessarily elaborate and expensive method of securing the action of D.A.D.P.S. in the body. Administration by injection, by preventing hydrolysis in the gut, may even reduce their therapeutic activity.

The administration of D.A.D.P.S. itself by mouth is safe, simple and very cheap. It seems to be the most rational form of sulphone treatment.

Reconsideration of the sulphone treatment of human tuberculosis may be advisable in the light of the findings recorded here. Preliminary observations show that D.A.D.P.S. treatment as here outlined is well tolerated by patients with tuberculosis of the lungs.

The Fate of the Foreskin

By D. GAIRDNER

(Abstracted from the *British Medical Journal*, ii, 24th December, 1949, p. 1433)

THE development of the prepuce is incomplete in the newborn male child, and separation from the glans, rendering it retractable, does not usually occur until some time between 9 months and 3 years. True phimosis is extremely rare in infancy.

During the first year or two of life, when the infant is incontinent, the prepuce fulfils an essential function in protecting the glans. Its removal predisposes to meatal ulceration.

The many and varied reasons commonly advanced for circumcising infants are critically examined. None are convincing.

Though early circumcision will prevent penile cancer, there is reason to suppose that keeping the prepuce clean would have a like effect in preventing this disease.

In the light of these facts, a conservative attitude towards the prepuce is proposed, and a routine for its hygiene is suggested. If adopted, this would eliminate the vast majority of the tens of thousands of circumcision operations performed annually in this country, along with their yearly toll of some 16 child deaths.

Artane Therapy for Parkinsonism

By L. J. DOSHAY

and

K. CONSTABLE

(Abstracted from the *Journal of the American Medical Association*, Vol. 140, 27th August, 1949, p. 1317)

TRIHENXYPHENIDYL (artane, 3-(1-piperidyl)-1-phenyl-1-cyclohexyl-1-propanol hydrochloride) is a new synthetic, antispasmodic drug for the treatment of parkinsonism.

Extensive pharmacologic tests with laboratory animals proved that action of the drug mildly resembles that of atropine in the control of sialorrhoea, in cycloplegic effects and cerebral stimulation. However, it is entirely free of the toxic effects of atropine on the cardiac vagus, blood pressure and circulation.

The results of clinical studies in a series of 117 patients treated with this agent established its great usefulness against parkinsonian disorders and its remarkable free disturbing side reactions. The investigation was conducted with 47 post-encephalitic, 33 idiopathic and 37 arteriosclerotic cases of parkinsonism, for periods ranging from six months to two years.

The drug was found on all scores to be a valuable addition to the drugs already in use for the treatment of parkinsonism. Besides the peripheral effects, common to other drugs, it has an unusual cerebral-stimulating action, which is particularly effective in combating the depression and inertia prevalent among these patients. It is, moreover, so remarkably devoid of toxic reactions that it is safe for use by the young

and the old, the ambulatory and the infirm, the hypertensive, the cardiac and the nephritic. It recommends itself as the drug of choice in arteriosclerotic and idiopathic cases, and should be regularly tried in post-encephalitic cases in which atropine or other forms of medication prove disturbing or ineffectual. As with other drugs, this compound is more effective when its use is combined with physical therapy and exercises.

Aureomycin Treatment of Amœbiasis

(From the *Journal of the American Medical Association*, Vol. 140, 27th August, 1949, p. 1344)

IN treating several cases of bacterial infection with aureomycin, McVay and his associates of the University of Tennessee noted alterations in the gross character of the stools. There was a definite reduction in the faecal bacterial count. This local effect led them to test the possible value of aureomycin in the treatment of amœbiasis, then prevalent in the Memphis area. Thus far 14 patients with amœbiasis have been treated with aureomycin. In a typical case both trophozoite and cystic form of *Endamoeba histolytica* were found in the stools of a patient suffering from para-umbilical pain, abdominal fullness and constipation. The patient was given 6.75 grains (439 mg.) of aureomycin orally in divided doses over a period of three days, at the end of which time his stool had become normal. The treatment was continued until the patient had been given a total of 21.75 grains (1,414 mg.) of aureomycin. During treatment the aureomycin blood level reached 8 micrograms per hundred cubic centimetres and all gastro-intestinal symptoms disappeared. Results of fourteen subsequent stool examinations over a period of three weeks have been negative. McVay believes that a much larger number of cases with adequate follow-up will be necessary before a final evaluation can be made of the value of aureomycin in the treatment of amœbiasis. The high aureomycin blood level observed in his cases leads him to believe that aureomycin therapy will be successful in extra-intestinal amœbic infections, such as hepatic abscess.

Aureomycin and Aluminum Hydroxide

By B. A. WAISBREN AND OTHER

(From the *Journal of the American Medical Association*, Vol. 141, 26th November, 1949, p. 938)

AUREOMYCIN given orally is effective in many microbial infections. The simultaneous oral administration of aluminum hydroxide gel and aureomycin will in some instances reduce the epigastric distress, nausea and vomiting that occasionally occur when aureomycin is given alone. A general inquiry indicates that it is a common practice to prescribe aluminum hydroxide gel with aureomycin. F. E. Di Gangi and C. H. Rogers of the College of Pharmacy of the University of Minnesota suggested that *in vitro* a suspension of aluminum hydroxide as an adsorbing agent might inactivate aureomycin. It was found that a solution of aureomycin that had been treated with aluminum hydroxide had little antibacterial activity. This prompted us to determine serum levels of aureomycin on 11 human subjects prior to and after they were given aluminum hydroxide gel with aureomycin. Ten of the subjects showed a decided drop in aureomycin serum levels within twenty-four hours after they were given 2 tablespoonfuls of aluminum hydroxide gel with each 0.5 gm. dose of aureomycin. These observations, which are being published in detail elsewhere,

demonstrate that the aluminum hydroxide gel interferes with absorption of aureomycin in the gut and may in certain infections lower the amount of aureomycin in the serum and tissues below an effective therapeutic level. Aluminum hydroxide gel should not be administered with aureomycin.

The Effect of Water and Salt Intake on Prickly Heat

By G. O. HORNE

and

R. H. MOLE

(Abstracted from the *Lancet*, ii, 13th August, 1949, p. 279)

PRICKLY HEAT is relieved by increasing fluid intake and reducing salt intake. It can be made to relapse by increasing the intake of table-salt.

The evidence suggests that the sodium ion is the effective agent in causing prickly heat.

Treatment of Herpes Zoster with Aureomycin

By M. L. BINDER AND OTHER

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 10th December, 1949, p. 1050)

To our knowledge there have not appeared any written reports on the use of aureomycin in the treatment of herpes zoster. It was by accident that we heard of the possible beneficial effects of aureomycin from a colleague. With this as a basis, we treated 4 patients who had herpes zoster with aureomycin, with the effective results recorded. This report is submitted in the hope that further investigation will produce equally good results in the treatment of a disorder which, in the past, has been so refractory in resisting all forms of therapy.

Epilepsy as a Sequela of Recurrent Malaria

By D. R. TALBOT *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 17th December, 1949, p. 1130)

CASES are presented in which chronic recurrent malaria was the probable causative agent of cerebral damage manifested by convulsive seizures and abnormal electro-encephalograms characteristic of epilepsy.

Chronic recurrent malaria must be considered in the differential diagnosis of convulsive seizures, and electro-encephalographic examination may be valuable for proper diagnosis.

Pathologic conditions of the central nervous system incident to the severe tropical type of recurrent malarial infection must be vigorously treated. In convulsive conditions such as those reported, treatment of the malaria is of primary importance. Until this is done, the use of anticonvulsive drugs must play a secondary rôle. Recent therapeutic progress in malaria provides an unprecedented opportunity to halt the process before further damage is done.

Aureomycin Therapy in Human Brucellosis due to *Brucella abortus*

By A. I. BRAUDE *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 19th November, 1949, p. 831)

AUREOMYCIN has been of benefit, immediately and consistently, to all the 40 patients treated in Minneapolis or at the Hospital Generale in Mexico, D.F. It appears to be dependable in the treatment of human brucellosis if the infection is caused by *Br. melitensis* or *Br. abortus*. Infections due to *Br. suis* have also been treated with aureomycin, but the number of reported cases is small.

A rough comparison can be made between the effectiveness of aureomycin and that of combined treatment with streptomycin and sulphadiazine. In table I two groups of 16 consecutive cases with treatment by each method are considered from the standpoint of clinical and bacteriologic relapses or failures. This comparison of aureomycin with a combination of streptomycin and sulphadiazine suggests that there is little difference in the over-all results in infections due to *Br. abortus*. In certain respects, however, the use of aureomycin is unquestionably superior to the combined use of the other two drugs. Aureomycin

TABLE I

Treatment of brucellosis due to Brucella abortus: Comparison of the results obtained using aureomycin with those obtained using a combination of sulphadiazine and streptomycin

	Aureomycin	Sulphadiazine-streptomycin
Period of observation ..	2 to 8 mo.	2 to 14 mo.
Total number of cases ..	16	16
Number of clinical relapses	2	1
Number of bacteriologic relapses or failures.	1	3

produces almost immediate improvement in the subjective well-being of the patient and a rapid fall in temperature. Its oral administration is easy and free from dangerous side effects. Hospitalization is not necessary. Treatment with streptomycin and sulphadiazine has not been consistently attended by rapid improvement in symptoms or fever, and the well-known side actions may be serious. Would there be any advantage of combining aureomycin therapy with streptomycin or dihydrostreptomycin, or with sulphadiazine? Heilman reported that the simultaneous administration of aureomycin and dihydrostreptomycin to experimentally infected mice reduced the numbers of *Brucella* organisms in the spleen more decidedly than did either agent alone. In observations made in this clinic, Magoffin, Anderson and Spink noted that the combination of aureomycin and streptomycin and aureomycin and sulphadiazine had a more pronounced anti-*Brucella* action in the chick embryo than did any one of the drugs when given alone. The only recorded observations in human subjects are those of Herrell and Barber, who administered a combination of dihydrostreptomycin and aureomycin to 4 patients with brucellosis. Two of the infections were due to *Br. suis* and 2 were due to *Br. abortus*. A satisfactory response to this combination of drugs was noted; and it was concluded that aureomycin and dihydrostreptomycin should be employed in the treatment of human brucellosis, although control data on the use of aureomycin alone were not reported. The present study, as well as that conducted in Mexico, D.F., indicates that in the routine treatment of infections due to

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(Abstracted from the *Journal of the American Medical Association*, Vol. 140, 27th August, 1949, p. 1317)

TRIHENXYPHENIDYL (artane, 3-(1-piperidyl)-1-phenyl-1-cyclohexyl-1-propanol hydrochloride) is a new synthetic, antispasmodic drug for the treatment of parkinsonism.

Extensive pharmacologic tests with laboratory animals proved that action of the drug mildly resembles that of atropine in the control of sialorrhœa, in cycloplegic effects and cerebral stimulation. However, it is entirely free of the toxic effects of atropine on the cardiac vagus, blood pressure and circulation.

The results of clinical studies in a series of 117 patients treated with this agent established its great usefulness against parkinsonian disorders and its remarkable free disturbing side reactions. The investigation was conducted with 47 post-encephalitic, 33 idiopathic and 37 arteriosclerotic cases of parkinsonism, for periods ranging from six months to two years.

The drug was found on all scores to be a valuable addition to the drugs already in use for the treatment of parkinsonism. Besides the peripheral effects, common to other drugs, it has an unusual cerebral-stimulating action, which is particularly effective in combating the depression and inertia prevalent among these patients. It is, moreover, so remarkably devoid of toxic reactions that it is safe for use by the young

and the old, the ambulatory and the infirm, the hypertensive, the cardiac and the nephritic. It recommends itself as the drug of choice in arteriosclerotic and idiopathic cases, and should be regularly tried in post-encephalitic cases in which atropine or other forms of medication prove disturbing or ineffectual. As with other drugs, this compound is more effective when its use is combined with physical therapy and exercises.

Aureomycin Treatment of Amœbiasis

(From the *Journal of the American Medical Association*, Vol. 140, 27th August, 1949, p. 1344)

IN treating several cases of bacterial infection with aureomycin, McVay and his associates of the University of Tennessee noted alterations in the gross character of the stools. There was a definite reduction in the faecal bacterial count. This local effect led them to test the possible value of aureomycin in the treatment of amœbiasis, then prevalent in the Memphis area. Thus far 14 patients with amœbiasis have been treated with aureomycin. In a typical case both trophozoite and cystic form of *Endamoeba histolytica* were found in the stools of a patient suffering from para-umbilical pain, abdominal fullness and constipation. The patient was given 6.75 grains (439 mg.) of aureomycin orally in divided doses over a period of three days, at the end of which time his stool had become normal. The treatment was continued until the patient had been given a total of 21.75 grains (1,414 mg.) of aureomycin. During treatment the aureomycin blood level reached 8 micrograms per hundred cubic centimetres and all gastro-intestinal symptoms disappeared. Results of fourteen subsequent stool examinations over a period of three weeks have been negative. McVay believes that a much larger number of cases with adequate follow-up will be necessary before a final evaluation can be made of the value of aureomycin in the treatment of amœbiasis. The high aureomycin blood level observed in his cases leads him to believe that aureomycin therapy will be successful in extra-intestinal amœbic infections, such as hepatic abscess.

Aureomycin and Aluminum Hydroxide

By B. A. WAISBREN AND OTHER

(From the *Journal of the American Medical Association*, Vol. 141, 26th November, 1949, p. 938)

AUREOMYCIN given orally is effective in many microbial infections. The simultaneous oral administration of aluminum hydroxide gel and aureomycin will in some instances reduce the epigastric distress, nausea and vomiting that occasionally occur when aureomycin is given alone. A general inquiry indicates that it is a common practice to prescribe aluminum hydroxide gel with aureomycin. F. E. Di Gangi and C. H. Rogers of the College of Pharmacy of the University of Minnesota suggested that *in vitro* a suspension of aluminum hydroxide as an adsorbing agent might inactivate aureomycin. It was found that a solution of aureomycin that had been treated with aluminum hydroxide had little antibacterial activity. This prompted us to determine serum levels of aureomycin on 11 human subjects prior to and after they were given aluminum hydroxide gel with aureomycin. Ten of the subjects showed a decided drop in aureomycin serum levels within twenty-four hours after they were given 2 tablespoonfuls of aluminum hydroxide gel with each 0.5 gm. dose of aureomycin. These observations, which are being published in detail elsewhere,

Conservative.—A large proportion of stones formed in the kidney escape spontaneously, while still very small stones which throw a shadow of not more than $\frac{1}{4}$ inch in diameter should be watched by x-ray, making an exposure at least once a month.

Intravenous urography will indicate the degree of back pressure and the need for intervention. One should seldom hasten to operate for a stone in a calyx. A stone which is held up in the upper lumbar ureter must be watched with frequent exposures, and the kidney damage may be estimated from these, whereas there need be no hurry about intervening for a stone in the lower end of the ureter. Calyceal stones in the elderly, debilitated or sufferers from intercurrent disease can generally be left with the assurance that they will do little harm. It has been gratifying to note how little increase in size has taken place in a stone in a calyx over a period of five years or more. One's hand may be forced however in any of the above conditions where severe infection has intervened.

Irrigation with Subey's solution.—Successes have been claimed for this method in certain recumbency cases; but in this group the stones tend to be passed when the patients become ambulatory, without such irrigation. For renal calculus generally, the method is unsatisfactory, unless carried out through a nephrostomy tube.

Bilateral stone.—When advanced on both sides these are generally better left alone. On the other hand it is sometimes advisable to remove the stones from both sides; certainly on separate occasions. It is wise to operate on the better side first; then at the second operation the question of nephrectomy can be more soundly decided, having previously actually handled the less damaged organ; for when one kidney is badly destroyed and the other is fairly sound, it is often proper to do a nephrectomy on the bad side. A severe infective complication of the worse kidney may necessitate operation on this side first.

TABLE I

Analysis of 223 operations on 174 consecutive personal cases of renal calculus

Nature of operation	Number of operations	Number of deaths	Percentage mortality
Pyelolithotomy	64	2	..
Nephrolithotomy	20	0	..
Combined pyelo- and nephro-lithotomy.	14	0	..
Plastic operation on pelvis and pyelolithotomy.	7	0	..
Excision of lower pole of kidney containing stone.	6	0	..
Excision of lower pole of kidney containing stone and ureterolithotomy on same side.	1	1	..
Permanent nephrostomy ..	8	2	..
Nephrectomy	96	4	..
Nephroureterectomy	5	0	..
Heminephrectomy	1	0	..
Combined nephro- and ureterolithotomy on same side.	1	0	..
Total number of operations ..	223	9	..
			4.03

Pyelolithotomy.—It is fortunate that in most cases when a stone has to be removed from the kidney, it is situated in the renal pelvis. The stone tends to be flattened from before backwards, with its lower edge near the lower margin of the pelvis, and for this reason an incision into the pelvis should be made along its lower border. Because of the position of the blood vessels anteriorly an approach to the posterior aspect of the pelvis gives the most convenient access. After removal of the stone a size 10 Charrière gum-elastic bougie is passed down the ureter into the bladder to be sure that there is no obstruction at a lower level. Interrupted five chromic sutures, passed so as not to include the mucous membrane, with a corrugated rubber drain stitched to the outside of the sutured line, complete the local requirements before closing the parietes.

Table I gives the details of my own cases.

Nephrolithotomy.—This is now done in a limited form; sometimes with multiple incisions, making these for preference through thinned portions of the parenchyma, when such are present. The incision should be made in the line of the main blood vessels of the incised region.

Suturing must be done with stout plain catgut passed with a large half-circle round-bodied needle; drainage should be as in pyelolithotomy. Radiography during the operation can be a helpful procedure, if all the facilities are at hand.

When the stone is seated in the lowest group of calyces and these are dilated, it is wise to amputate the lower pole of the kidney. By removing the renal tissue as a wedge, the remaining cut surfaces come together without difficulty. The sutures and needles just described should be used. These should be passed about $\frac{1}{2}$ inch apart entering the renal substance about the same distance from the free edge of the cut surfaces. Ligation of the vessels of the lower pole is a needful preliminary to the excision. A drain should be placed down the suture line.

Nephrectomy.—When the opposite organ is found to be sound, a dilated kidney especially if infected should be removed. It is a great mistake to leave behind a kidney which will be a source of ill health.

Nephrostomy.—In some cases of bilateral disease, the establishment of kidney drainage on both sides in a permanent form can put years on to the patient's life and should therefore be considered in advanced cases.

Conclusions concerning operations.—In this series mortality for operations on the kidney for stone has been kept low (4 per cent) by consistently observing two essential needs:

1. Avoiding pre-operative bladder instrumentation especially with regard to passing ureteric catheters; intravenous urography invariably supplies enough information for the decisions concerning operation to be made.
2. Strict attention to post-operative drainage down to the site of incision into the kidney.

Cancer of the Breast

(From the *Medical Press*, Vol. 223, 4th January, 1950, p. 4)

THE treatment of cancer of the breast is always a problem and practitioners are always asking for information concerning the value of x-ray therapy following operation. H. Gleen Bell of San Francisco has carefully followed up a series of cases in the University of California Medical Centre. Some 736 cases of cancer of the breast were treated between the years 1930-44. From this study the author is convinced that x-ray therapy as an adjunct to the surgical treatment of carcinoma of the breast has not significantly increased the five-year survival rate.

This conclusion has been reached by a number of British surgeons, and it should be realized by the rank and file of the profession.

BAL and Uranium Poisoning

(From the *Medical Press*, Vol. 222, 21st December, 1949, p. 574)

THE effectiveness of BAL (2:3-dithiopropional) in the treatment of heavy metal poisoning (e.g. arsenic and mercury poisoning) is now well known. The basis of the therapy is the strong affinity of the —SH groups of the BAL for the metallic ions, preventing combination of the metals with the sulphydryl groups of tissue enzymes.

This, however, is not the case in uranium poisoning, where BAL was found to be completely ineffective in modifying the course of systemic uranium poisoning in rats. Indeed it has been reported that BAL actually enhances the toxicity of uranium in dogs. These results indicate that uranium exerts its toxic effects primarily by some other means than a combination with sulphydryl groups.

The increasing use of uranium in the manufacture of atomic piles, etc., focuses attention on the possibility of uranium poisoning, and it appears from the above experiments that BAL will not be an effective agent in the treatment of such a condition.

Toleration of Contact Lenses

(From the *Medical Press*, Vol. 222, 21st December, 1949, p. 575)

A. G. CROSS reports the results of a questionnaire sent to 875 contact lens wearers. The lenses had been prescribed by four independent fitters. The outstanding fact emerges that one-third of the total number of persons fitted with contact lenses had ceased to use them. The reasons given were variable, but in the majority of cases the patients complained of extreme discomfort, or of blurring of vision (Sattler's veil). This blurring was noted from time to time in 39 per cent of all the cases, and the causation is not yet worked out. Other patients gave various excuses for not wearing their contact lenses such as 'No time to preserve and get used to them', or redness of the lids. Some patients complained that their lenses did not fit, but this can only be a statement of opinion, since in the opinion of the fitters they did fit or they would not have been supplied.

More than half the lenses ordered were in cases of myopia, while the two next largest groups were mustard-gas keratitis and keratoconus.

Benefits reported from contact lenses were the avoidance of visible spectacles, a wider field of vision, absence of light reflections, convenience for sportsmen, actors and musicians.

It will be seen that contact lenses should not be prescribed without explanation to the patients that they have certain disadvantages and inconveniences.

Thoracic Complications of Amœbiasis

(From the *Medical Journal of Australia*, Vol. II, 24th December, 1949, p. 920)

ROBERT SHAW (*Surgery, Gynaecology and Obstetrics*, June 1949) states that of the general population of America 20 per cent are infested with *Entamoeba*

histolytica. Hepatic abscess will complicate 5 per cent of such infestations and the thoracic cage will be involved in 15 per cent of patients with liver abscesses. Amœbic abscess occurs fifteen times more commonly in men than in women; the majority of those affected are aged between twenty and fifty years. The hepatic abscess is usually single and in the right lobe of the liver. Thoracic complications arise from spread into the pleural cavity or into the lung. Abscesses of the left lobe may extend into the pericardial sac. Solitary amœbic abscesses have been described; they are rare and probably embolic. In half the cases with pleuro-pulmonary complications there is no history of dysentery. The usual complaint is of pain in the right side of the chest and shoulder, of an unproductive cough and later of hæmoptysis, which precedes the anchovy paste sputum. There is a septic fever and the usual evidences of infection appear. A radiograph characteristically shows the localized elevation of the diaphragm, which is best seen in the lateral view. If there is extension into lung, a shadow is seen involving the lower lobe and tapering to the hilum, with or without the signs of an abscess; if into the pleural space, there will be the signs of pleural exudate. Loculation is common with amœbic empyema. The mortality is high, less when the lung is involved without an empyema and least when a broncho-hepatic fistula has occurred without empyema or pulmonary abscess. Emetine is given, one grain intramuscularly for six to ten days. Aspiration of the liver abscess should be done, if possible. Surgery is indicated in pleuro-pulmonary complications when secondary infection has occurred, when an empyema is present and does not respond to aspirations, when a broncho-hepatic fistula persists, or when pulmonary fibrosis consequent on the abscess is producing symptoms.

Simulated Homicide

(From the *Medical Journal of Australia*, Vol. II, 12th November, 1949, p. 722)

A NICE example of the fallacious conclusions which can result from a combination of circumstantial evidence and unsatisfactory post-mortem medical examination has been reported by Joseph W. Spelman. The story was that early one morning, the police were notified that an apparently intoxicated Negro man, accompanied by two women, had been seen carrying through the streets a carelessly wrapped parcel, which appeared to contain the body of a dead child. A passer-by reported overhearing the trio discussing the best means of disposing of the corpse. On arrival of the police, the man stated that the body was that of his son, aged sixteen months. The body was immediately taken to a mortuary by the police and the medical examiner notified. The mother of the dead child was a patient in a neighbouring hospital. The father stated that he had put the boy to bed on the sofa in the family living room at about 10 o'clock the night before. He had then gone to the apartment of one of the women, got drunk, and returned home at 2-30 a.m. to find his son dead on the floor near the sofa. After a conference between the father, his companion of the night and another woman, the three of them wrapped the body in a blanket and were proceeding along the street aimlessly when detected at 3 a.m.

At post-mortem examination the body was found to be dressed in urine-soaked daytime clothing. The shoes had been placed on the wrong feet and were laced, though the laces were not tied. The body was undernourished and underdeveloped. There was no external evidence of recent trauma. Incision of the body revealed marginal pulmonary emphysema and occasional subpleural petechiæ. Under the scalp a large transverse linear fracture of the right parietal bone was found, covered by a fresh hæmatoma. A

scanty epidural hæmorrhagic extravasation surrounded the fracture. There were a few superficial petechiæ throughout the cerebral cortex. If, as Spelman points out, the autopsy had been concluded at this point, there would have been a strong presumption that the child had died as a result of a fractured skull with associated cerebral damage, and this with the peculiar circumstances of the story, might well have led to a charge of homicide. However, the examination of the body was continued, and the larynx was found to be completely obstructed by multiple papillomatous tumours. These soft, friable, polypoid masses had obliterated the vocal cords and extended from the ventricular ligaments to the inferior margin of the cricoid cartilage; firmly attached to the circumference, the neoplasm had displaced the submucosa and had penetrated to, but not into, the laryngeal cartilages. It was later learned that the child had been examined in a children's clinic at the age of ten months because of hoarseness, muffled voice and loss of weight, and again at the age of thirteen months when increase of weight was noted, but nothing was recorded regarding the muffled voice and hoarseness; the larynx had never been directly examined. The final inference was that the child at the time of death had an upper respiratory tract infection, and that the resultant œdema, hyperæmia and exudation, superimposed on pre-existing partial laryngeal obstruction, brought about sudden occlusion. The fracture of the skull could be explained as having been sustained during the agonal period, either from a fall from the sofa or from trauma received during a terminal asphyxial convulsion. The father and his companions presumably became afraid and being duddled, acted foolishly, so making the circumstantial evidence many times more damning. A better illustration of the importance of complete and thorough medico-legal autopsies would be hard to find.

certain disadvantages and dangers associated with hyoscine. At the onset of sea-sickness the patient should lie flat for half an hour and take 100 milligrammes of 'Anthisan'. When this has taken effect he should get up; while the sea remains rough he should eat light meals, restrict fluids and keep warm. 'Anthisan' (100 milligrammes) should be taken three times a day as long as necessary.

Much more impressive results, however, have come from America. L. N. Gay and P. E. Carliner of Johns Hopkins Hospital and University, Baltimore, have been studying the effects of 'Dramamine' (B-dimethyl-amino-ethyl benzohydryl ether 8-chloro-theophyllinate). During trial of the drug in the treatment of hay fever and urticaria, it was found to provide consistent and complete relief to a woman who had suffered all her life from ear sickness. A controlled experiment was then carried out in 485 soldiers in an army transport ship during a rough passage across the Atlantic. Altogether on the voyage 372 of 389 men with sea-sickness were completely relieved of symptoms within one hour after the first dose of 100 milligrammes of 'Dramamine'; 17 derived only partial or no relief. A dose of 100 milligrammes taken every five hours and before retiring was effective; when necessary, the drug was given *per rectum*, with completely satisfactory results. No undesirable reactions were experienced in any case.

Streptomycin Treatment of Ozena

By K. M. SIMONTON

(From the *Proceedings of the Staff Meetings of the Mayo Clinic*, Vol. 24, 8th June, 1949, No. 12, as abstracted in the *Journal of the Philippine Medical Association*, Vol. 25, August 1949, p. 409)

THE treatment of ozena remains one of the unsolved problems of rhinology.

Briefly, the pathologic changes consist of marked decrease in the connective tissue of the submucosa, with obliteration of the blood vessels, trophic changes in the nerves, diminution or complete destruction of the glandular elements and metaplasia of the epithelium from ciliated columnar to the stratified squamous type. As a result of these irreversible changes, there is exudation of thick green tension pus which on drying forms crusts. Bacterial action on the crusts produces an offensive odour which is most distressing to the patient and his associates.

The ætiology of the disease is unknown. It has its onset in childhood, usually reaching maximal intensity at puberty and often subsiding spontaneously at middle life. Extensive bacteriologic studies have failed to reveal of specific cause for the condition, although among the organisms regularly found in advanced cases of ozena is *Klebsiella*, which is regarded as a secondary invader.

The types of treatment may be divided into three groups.

Cleansing the nasal cavities by irrigation removes the crusts, and gives temporary relief and application of hygroscopic solution like corn syrup or 25 per cent dextrose in glycerine reduces crusting and odour. Spraying the nose with oil delays the reformation of crusts. Estrogenic substances when added to the oil used for spraying the nose produce temporary improvement owing to hyperæmia of the nasal mucosa.

Immunologic therapy.—Vaccines from various organisms have not proved successful. Surgical treatment has been devised to reduce the volume of the nasal chambers and others to form adhesions between the septum and the lateral wall of the nose. Cervical sympathectomy and the Leriche operation of stripping

Multiple Amœbic Abscess of the Lungs

By P. K. CHATTERJEE

and

S. SEN GUPTA

(Abstracted from the *Journal of the Indian Medical Association*, Vol. 18, September 1949, p. 481)

A CASE of multiple amœbic abscess of the lung has been described.

The diagnosis was confirmed by finding *Ent. histolytica* in the sputum.

The frequency and pathogenesis of pulmonary complication of amœbiasis are discussed.

Motion Sickness

(Abstracted from the *Medical Journal of Australia*, Vol. II, 23rd July, 1949, p. 140)

THE main standby in the treatment of motion sickness for a good many years has been hyoscine. A further war-time discovery was the thiobarbiturate known as V12. Now antihistamine drugs have been pressed into service in this field with rather striking results. M. B. McEvedy, following up a chance observation that patients in a ship's hospital who were under treatment with antihistamine drugs seemed unaffected by sea-sickness, carried out a comparison experiment with 'Anthisan' (pyranisamine malcate) and hyoscine. 'Anthisan' appeared to be at least as acceptable as hyoscine to those liable to be sea-sick, and is free from

the sympathetic nerve fibres from the common carotid artery has found temporary favour in the Latin countries.

Heilman in 1945 reported successful inhibition of growth of several strains of *Klebsiella* by the use of streptomycin. Thornell in 1946 demonstrated *Klebsiella* in pus and tissues of 7 cases of ozena.

The author reports eight cases of ozena treated with streptomycin in all of which the presence of *Klebsiella* was demonstrated.

Symptomatic improvement occurred in 7 of the 8 patients at the time of treatment. Five reported definite subjective improvement; one has not been improved.

The *Klebsiella* became resistant to the action of streptomycin in 2 cases. In one case the dose of 1,000,000 units a day was deemed inadequate.

Infection in this sinuses should be treated at the time of streptomycin therapy for ozena.

Streptomycin was given 1 gm. daily by intramuscular injection and 0.5 to 1.0 gm. of streptomycin daily by nebulization. Initial response to treatment was favourable in each case.

The group of cases is too small to draw definite conclusions from, concerning the value of streptomycin therapy in atrophic rhinitis associated with ozena. Suppuration, the formation of crusts and the symptoms of infection in the atrophied nasal mucosa have been subjectively improved for periods of eight to forty-two months in 5 of the cases.

This result is encouraging and warrants further trial of streptomycin in the treatment of this condition.

An Improved Swab for the Detection of Threadworm Ova

(From the *Physician's Bulletin*, Vol. 14, November-December 1949, p. 178)

BOYCORR has described a swab for use in the detection of threadworm ova which appears to have certain advantages over the N.I.H. swab. The swab consists of a wooden tongue depressor, 6 inches by $\frac{3}{4}$ inch; a strip of cellophane the size of a microscope slide, approximately 3 inches by 1 inch, doubled over the end of the depressor and held in place by several turns of a rubber band; and a paper envelope (a 'pay envelope', 2 inches by 4 inches, is suitable).

The swab should be rubbed along the perianal folds with pressure just short of causing pain. It is then replaced in the envelope, on which it is convenient to write the patient's name. In the laboratory the cellophane is removed opened out, and placed on a slide; a drop of Canada balsam between the slide and the cellophane helps to keep the surface flat. Examination should be made under the $\frac{2}{3}$ -inch objective and may be concentrated in the areas showing epithelial and faecal debris.

The single crease in the cellophane, its strength, and the ease with which the swab can be packed, have been found to be improvements over the N.I.H. swab.

Treatment of Glaucoma

(From the *Medical Journal of Australia*, Vol. I, 14th January, 1950, p. 56)

LOUIS LEHRFELD (*Archives of Ophthalmology*, September 1948) maintains that every patient with glaucoma should be treated medically until such time as control of intraocular pressure is no longer maintained at a limit at which visual acuity and visual

fields may be conserved. Acute congestive glaucoma should be treated intensively medically for twenty-four hours and surgery resorted to if tension has not been reduced. However, if reduction in tension under intensive miotic therapy is such as to bring about a return to normal vision, surgery may be deferred. The treatment of chronic congestive glaucoma is medical. Control of intraocular tension in this category does not mean a reduction to normal, but consists in reduction to a degree which the eye in question will tolerate. If the patient has repeated exacerbations of increased intraocular pressure with symptoms, operation should be performed. The author recommends a basal iridectomy if the eye is red, an iridencleisis if it is only mildly infected, and an Elliot trephination if it is 'quiet'. For chronic simple glaucoma he prefers medical treatment even if the vision is not normal, the visual fields are cut down and the tension is not normal. He finds that 70 per cent of all patients with chronic simple glaucoma can be made comfortable, and surgery is performed when miotics are failing and the patient is losing his vision; in these cases the operation of choice is iridencleisis. He makes the point that before operating on patients with chronic simple glaucoma, the surgeon should remember that old people prefer a little sight with glaucoma to a blind eye that apparently has been cured of glaucoma.

Reviews

OBSTETRIC ANALGESIA AND ANÆSTHESIA: THEIR EFFECTS UPON LABOUR AND THE CHILD.—By F. F. Snyder, M.D. 1939. W. B. Saunders Company, Ltd., Philadelphia and London. Pp. viii plus 401. Illustrated

THERE are seventeen chapters of packed information in this book. The subject-matter is divided into two sections. The first section deals with the respiratory injuries of the child. The entire book consists of 385 pages and of these the first section consists of 212 pages. Says the author in the preface: 'Since all drugs commonly given for the relief of pain tend to alter the functioning of respiration, thus striking the foetus at the point of maximum susceptibility . . . there is detailed inquiry about the principal types of pathologic alterations of respiration, e.g. Asphyxia, Atelectasis and Pneumonia'. Here is the explanation of the detailed account of foetal respiratory complications included in a book meant to deal with anaesthetics and analgesics in labour.

The principal anaesthetics have been dealt with more from a laboratory point of view. The practising anaesthetist may not always find the clinical information which he might be seeking. The chapter dealing with narcotic gases does not contain sufficient information. Special anaesthesia has been dealt with in an abridged fashion.

The printing and get-up of the book are excellent. The great use of the book will be for him who wants academic and experimental references about the action and after-effect of any particular anaesthesia he may be using. It is the type of book to be kept in a library for the use of anaesthetists, obstetricians and paediatricians.

M. N. S.

RECENT ADVANCES IN PHYSIOLOGY.—By W. H. Newton. Seventh Edition. 1949. Published by J. and A. Churchill Ltd., 104, Gloucester Place, London, W.C.1. Pp. 268 with 90 illustrations. Price, 21s.

SINCE the publication of the last edition of this book, a vast amount of literature has accumulated, but

Professor Newton has not attempted to survey the wide field, for many such reviews are already available. His aim is not to impart the greatest amount of knowledge, but rather to indicate to the student modern currents of thoughts. To this end he has selected subjects of interest and importance, and these are recorded and evaluated in this edition. The subjects chosen are temperature regulation, water diuresis, digestion, physiology of pregnancy, blood pressure and kidneys, cardiac catheterization, electric excitation of nerve, cutaneous sensation, auditory impulses and colour vision. All the chapters are new.

R. N. C.

THE RAT IN LABORATORY INVESTIGATION BY A STAFF OF TWENTY-NINE CONTRIBUTORS.—

Edited by Edmond J. Farries, Ph.D., and John Q. Griffith, Jr., M.D. Second Edition. 1949. Published by J. B. Lippincott Company, Philadelphia and London. Pp. 542 with 179 illustrations. Price, £5 5s. net

This book has been contributed by twenty-nine authors for workers employing the rat in laboratory investigation. It contains a wealth of material from breeding and care to anatomy, physiology and diseases of rats together with various methods and procedures which have proved satisfactory in laboratory. There is an interesting chapter on the method of investigation of behavioral phenomena in the rat. In another chapter entitled 'Surgery of the rat', various operative procedures are clearly described. The book will be invaluable to those engaged in laboratory research.

R. N. C.

NORMAL VALUES IN CLINICAL MEDICINE.—By F. William Sunderman, M.D., Ph.D., and Frederick Boerner, V.M.D. 1949. Published by W. B. Saunders Company, Ltd., Philadelphia and London. Pp. xxx plus 845 with illustrations. Price, 70s.

'When you can measure what you are speaking about and express it in numbers, you know something about it; when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind'. This book serves to fill a gap that medical men often come across. It presents discussion and compilation of 'normal' values. The data have been selected and condensed from relevant literature on the advice of collaborators in almost all branches of clinical investigation. The book is divided into sections, according to body systems, the last section dealing with miscellaneous data including statistical methods, food values, doses, weights and measures, etc. There is a bibliography at the end of each chapter so that one may readily refer to the original. The book is bound to be a valuable source of convenient reference for both doctors and students.

R. N. C.

PRINCIPLES OF MEDICAL STATISTICS.—By A. Bradford Hill, D.Sc., Ph.D. Fifth Edition, Revised and Enlarged. 1950. Published by the Lancet Limited, 7, Adam Street, Adelphi, London. Pp. lx plus 282. Price, 10s. 6d. net

In this edition which has followed the enlarged previous edition after only one year extensive changes have not been made. The only significant addition consists of 25 exercises, complete with their solutions and covering 27 pages towards the end.

The essential features of this book have always been: (1) Emphasis on the Sherlock Holmes aspect of the situation. That is how unsuspected incomparability between samples believed to be comparable is brought out. An example is a house sampling undertaken in England in 1919. The intention was to inspect every 5th house so far as possible. The houses which were found closed at the time of the visit were

ignored. But houses with children are less often found closed than those with adults only. The samples were, therefore, not representative of the 'universe' of houses in this area. This important consideration has obviously nothing to do with mathematics of which an average medical man is not particularly fond. Another example gives various reasons for chances of recovery from appendicitis in hospital. (2) Presentation of statistics. Need for tabulation is explained and so is the inferiority of diagrams and graphs. (3) Examination of arithmetical terms like the average, median mode, variability given in a lucid style. (4) Subtler procedures like sampling with its rules and tests, including χ^2 . (5) Common fallacies and difficulties in calculations. (6) Standard tables, etc.

All important items have separate chapters allotted to them and every chapter has a summary.

Medical men intending to present figures to the profession will do well to obtain and read this little book, even if they are in a position to have their work analysed by a professional statistician. The latter because of his lack of interest in or touch with clinical matters may miss a point in Sherlock Holmesing on diseases and disabilities which are after all better known to the clinicians.

An excellent publication.

S. D. S. G.

Correspondence

PENICILLIN TREATMENT OF GLYCERINE VACCINE LYMPH

SIR,—With reference to the comment on my letter by Dr. Das Gupta in December (1949) issue of the *Indian Medical Gazette*, I submit that I may be permitted to answer all the points raised by him, one by one, in view of the great importance of the subject.

(1 and 2). No mention is made in my letter to the effect that there is any increase in the bacterial count but that the bacterial content already present in the penicillin-treated lymph show up once the residual penicillin from the lymph is either inactivated or removed completely.

(3). Field tests with penicillin-treated lymphs were not done by me for the obvious reason that the associated bacteria are quite alive and only masked by penicillin.

(4) I beg to differ from Dr. Das Gupta in that the bacterial content of the glycerine vaccine lymph will increase at room temperature in view of the lymph being organic matter. I need hardly point out that the glycerine in the vaccine lymph is bacteriostatic and mildly bactericidal except only for fungus and so does not permit any such increase in the bacterial content. This vital point has missed his attention.

(5) Dr. Das Gupta has suggested without giving any reason that my centrifuge experiments seem fallacious. I am sure no body will expect experimental details to be described in a small letter like the one in the August issue. He will however know the full details soon after the publication of the entire article, which is in the press*.

(6) Penicillin is bacteriostatic to bacteria in nutrient fluids and bactericidal in non-nutrient media as shown by Cnam and Duthie (1945). Glycerine vaccine lymph being a non-nutrient medium, the action of penicillin there is only bacteriostatic.

* Published in *J. I. M. A.*, May 1950 issue. Opinions from other workers are also invited.—Editor, *I.M.G.*

(7) Caution is warranted while using penicillin-treated lymph on humans as the meagre amount of penicillin present in the lymph may be reduced to ineffective concentrations in the body after getting highly diluted by the body fluids on absorption after vaccination. This will permit the organisms of the lymph to thrive and multiply and thus render the penicillin-treated lymph unsuitable for vaccination.

Lastly, is it or is it not rational that when one is dealing with a mixture of inhibiting and inhibited substances, each has to be separated from the other before sterility tests are conducted?

Yours faithfully,
V. N. KRISHNAMURTHY,
Superintendent,
Vaccine Institute.

BANGALORE CITY,
28th March, 1950.

REFERENCE

CHAIN, E., and DUTHIE, E. S. (1945). *Lancet*, i, 652.

A NOTE ON FILING MEDICAL JOURNALS

SIR,—Many of us subscribe to the medical journals and some desire to maintain them filed for future reference. It is usually done by binding the issues in individual volumes with volume-index attached in the beginning. I have been doing so for some years, but after realizing great inconvenience thereby, have adopted a different method which has proved useful to me. At the recommendation of my friends who realized the benefits of this method, I dare to publish it for the use of those to whom it may appeal. There is nothing much novel about it, but the convenience may not occur to everybody and hence this communication.

The inconvenience in the usual method arises from having to handle bulky volumes, one after another, for searching references on a desired subject. Once the inconvenience is felt, the remedy is simple enough. The indices of serial volumes are filed and later bound together in a volume the index-volume. The issues are stripped of advertisement pages, leaving the date and index of the issue intact. The serial issues forming a volume are kept in a card-board box prepared for it, or in a file. The boxes may be locally prepared and are of the type of file cases supplied by the *Journal of the American Medical Association* for its journal. The files may be of the type supplied by the Easibind Ltd. of London. If economy is desired without sacrificing efficiency, a piece of a card-board of the size of the journal is placed above and below each volume of the stripped issues and it is tied firmly by a string. The number of the volume and the year are written on the covering card-board to facilitate reference. Of course, in every case due precautions should be taken to see that the volume does not become the prey of insects.

Advantages accruing from this method are :—

1. The particulars of the required issues can be obtained by referring to the index-volume which should not be made bulky.
2. Desired issues can be removed from the volume and studied conveniently. A bulky volume need not be handled with unavoidable inconvenience and awkwardness inherent to the bulk.
3. Total cost of maintenance of the journals by the 'economic method' is insignificant. The cost assumes a sizeable figure when a number of journals are to be maintained by the usual method.

Yours faithfully,
P. L. DESHMUKH, M.D.,
D.T.M. & H., F.C.P.S.,

Honorary Physician, Sassoon Hospitals.

PRECAUTIONARY MEASURES IN THE MANAGEMENT OF PNEUMONIC PLAGUE

SIR,—In the valuable article by Prof. Seal on pneumonic plague in your April 1949 issue, under the precautionary measures, no mention is made of the importance of protecting the eyes against droplet infection by the use of well-fitting goggles by all contacts of the patient by doctors and nurses. The conjunctival mucous membrane is a very vulnerable point, and infection is known to have resulted in spite of face masks in the absence of goggles.

Yours faithfully,
P. A. DALAL, L.M.S., D.T.M. & H.

BOMBAY 4,
4th May, 1950.

I appreciate the suggestion made by Dr. Dalal who, I know, is an old worker on plague. Although there is no evidence on record to show that the pneumonic plague infection could occur through the human conjunctiva, the use of goggles as an extra precautionary measure has been advocated in certain textbooks and would certainly be helpful. The cases of infection which Dr. Dalal is thinking to have occurred through conjunctiva in spite of the face mask were probably due to the defect in the mask, as pointed out clearly by Wu Lien in his book on Pneumonic Plague (1926). There is, however, a possibility of droplets of infective material (e.g. sputum, post-mortem material, etc.) to get into the nose through the naso-lacrimal duct and thus cause infection.—S. C. S.]

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CONTENTS

	Page		Page
ORIGINAL ARTICLES		FOUR NEW OFFICERS ARRIVE AT W.H.O. REGIONAL OFFICE 311	
Amoebic Abscess of the Brain. By P. Koshy, B.A., M.D. 287		RECORD PRODUCTION OF RADIO-ACTIVE ISOTOPES 311	
Madura Foot (Mycetoma). By L. M. Ghosh, N. C. Dey and D. Panja .. 288		INDIAN COUNCIL OF MEDICAL RESEARCH .. 311	
Treatment of Kala-azar with Methyl Glucamine Antimoniate. By P. C. Sen Gupta, M.B. (Cal.) 291		BACK-ROOM-BOYS OF MEDICINE GET NEW HEADQUARTERS 312	
Laboratory Diagnosis of Scrub Typhus. By T. V. Swamy, M.B., B.S. .. 297		UNESCO COUPON SCHEME 312	
Advent of Elkosin. By Binoy Banerji, M.B., L.M. 298		PRECISION INSTRUMENTS UNDER CONSTRUCTION IN DELHI LABORATORY RECORDINGS DURING HUNDRED THOUSANDTH PART OF A SECOND MAIN LINES OF SCIENTIFIC RESEARCH IN NATIONAL INSTITUTES 312	
The Antibacterial Principle of the Betel Leaf. A preliminary report. By M. Narayana Pai and Miss R. J. Irani .. 302		NEW USES FOR PLASTICS. By Trevor I. Williams 314	
A MIRROR OF HOSPITAL PRACTICE		SIR EDWARD MELLANBY 314	
Reiter's Disease. By S. Pramanik, M.B., D.T.M. (Cal.) 304		CLIFFORD DOBELL, M.A., ScD., F.R.S. .. 315	
A Case of Accidental Paludrine Poisoning. By Paresh Chandra Sen, L.M.P. .. 305		COLONEL H. E. SHORTT, C.I.E., I.M.S. (Retd.) 316	
A Case of Myiasis of the Nasal Cavity. By Surjya Kumar Bhowmick, L.M.F. .. 306		CANCER HOSPITAL IN CALCUTTA .. 316	
EDITORIAL		PRESS INFORMATION BUREAU, MINISTRY OF INFORMATION AND BROADCASTING, GOVERNMENT OF INDIA, CALCUTTA 316	
Abreast with the Times 307		PUBLIC HEALTH SECTION	
MEDICAL NEWS		Maternity and Child Welfare Work in Railway Colonies. By B. L. Chopra, D.P.H., D.T.M. (Liverpool) .. 317	
ELEVENTH INTERNATIONAL DENTAL CONGRESS. Fédération Dentaire Internationale, LONDON, JULY 1952 .. 308		Note on Diet Surveys carried out in the Central Provinces and Berar. By D. M. Roy 320	
THIRD WORLD HEALTH ASSEMBLY .. 309		Use of Defatted Groundnut Cake Flour as Food. By S. B. Lal and A. Bose .. 322	
W.H.O. MALARIA PROJECT IN AFGHANISTAN TO BE LAUNCHED BY INDIAN EXPERTS .. 310			
INDONESIA JOINS THE S.-E. ASIA REGIONAL ORGANIZATION OF W.H.O. 310			

(Continued on page 286)

CONTENTS—(Continued from page 285)

	Page		Page
FIFTY YEARS AGO		AUSCULTATORY RESPIRATORY MURMUR	
CORRESPONDENCE (<i>Indian Medical Gazette</i> , July 1900, Vol. 35, p. 277).		(<i>Journal of the American Medical Association</i> , Vol. 141, 24th December, 1949, p. 1238)	330
THE HOMŒOPATHIC MEDICAL SCHOOL	326		
FILARIAL METAMORPHOSIS IN THE ANOPHELES	326	REVIEWS	
A GARBLED QUOTATION	326	VITAMIN A REQUIREMENT OF HUMAN ADULTS (M.R.C. SPECIAL REPORT SERIES No. 264, 1949)	331
THE VALUE OF 'SAGS' AS ANTI- SCORBUTICS IN THE JAIL DIETARY	327	THE EYE MANIFESTATIONS OF INTERNAL DISEASES. <i>By I. S. Tassman, M.D.</i> <i>Second Edition.</i> 1946	331
CURRENT TOPICS, ETC.		TEXTBOOK OF HISTOLOGY. <i>By Alexander A. Maximow and William Bloom.</i> <i>Fifth Edition.</i> 1948	331
WORLD BRAILLE—AN ADVANCE TOWARD ONE WORLD. <i>By Percy Winner</i> (UNESCO Features, No. 19, 15th April, 1950, p. 10)	327	PATHOLOGY. <i>Edited by W. A. D. Anderson, M.A., M.D., F.A.C.P.</i> 1948	331
THE OSLO SCHOOL BREAKFAST. <i>By Ruth Sachs</i> (UNESCO Features, No. 20, 1st May, 1950, p. 7)	328	TEXTBOOK OF BACTERIOLOGY. <i>By William Burrows, Ph.D.</i> <i>New (15th) Edition.</i> 1949	332
EARTH GROWING WARMER, NOT COLDER, UREY SAYS (<i>Chemistry and Chemical Engineering in the United States</i> , March 1950)	329	LEPROSY: FACTS AND FICTION. <i>By D. N. Mukerjee</i>	332
ADSORPTION OF AUREOMYCIN BY ALUMINUM HYDROXIDE GEL	329	BOOKS RECEIVED	332
AN INCOMPATIBILITY BETWEEN VITAMIN B ₁₂ AND ASCORBIC ACID	329	ABSTRACTS FROM REPORTS	
A COLORIMETRIC ASSAY FOR ANTIHISTAMINES	329	ANNUAL REPORT OF THE TUBERCULOSIS RELIEF ASSOCIATION, 73, DHARAMTOLA STREET, CALCUTTA 13	332
NEW ANTACIDS—ALUMINUM GLUTAMATES	329	P. G. SINGHANEE HINDU HOSPITAL, GRANT ROAD, BOMBAY	333
STERILIZATION OF CLINICAL THERMOMETERS (<i>Journal of the American Medical Association</i> , Vol. 141, 24th December, 1949, p. 1272)	330	ANY QUESTIONS	
EPIDEMIC OF CAVE-BORNE PULMONARY INFILTRATIONS WITH EOSINOPHILIA (<i>Journal of the American Medical Association</i> , Vol. 141, 24th December, 1949, p. 1259)	330	TREATMENT OF THREADWORMS AND OF STAMMERING	333
		PHYSICAL THERAPY JOURNALS	334
		SERVICE NOTES	334

Original Articles

AMŒBIC ABSCESS OF THE BRAIN

By P. KOSHY, B.A., M.D.

(Department of Medicine, Christian Medical College, Vellore)

AMŒBIC abscess of the brain is one of the rarest and most fatal of the complications of amœbiasis. In the majority of cases described brain abscess has followed an abscess of the liver or lung. Craig (1944), in his forty years of study of amœbiasis, says he never saw a case of amœbic abscess of the brain except as a museum specimen.

The statistics of the Medical College Hospital, Vellore, show from 1944 to 1949 there were 2,275 cases treated for amœbic dysentery and there were 166 cases of amœbic abscess of the liver among them. During this period there was not a single case of amœbic abscess of brain recorded. Of the 561 post mortems performed in the above hospital there were only 8 cases of amœbic dysentery and one of amœbic abscess of the liver.

Reddy and Thangavelu (1948) in an analysis of 2,641 cases of dysenteries treated in Madras General Hospital recorded 1,011 cases of amœbic dysentery of which 44 came for post mortem and found no case of amœbic abscess of the brain. In a recent review of 104 post mortems of metastatic brain abscess by Gates *et al.* (1950) there is not a single case mentioned of amœbic abscess of the brain.

Amœbic abscess of the lung may be primary, reaching the organ through the blood stream, or secondary to an amœbic abscess of the liver. It occurs in 10 per cent (Kartulis, 1904) to 20 per cent (Rogers, 1922) of liver abscess cases. Craig quotes the incidence as 3 in his series of 26 cases of liver abscess and in 5 cases liver abscess ruptured into pleural cavity producing empyema.

Well known among the complications of amœbic colitis is abscess of the liver. According to Simonds (1843) its incidence ranges from 3.48 in surviving patients to 42.36 per cent in cases in which necropsies were performed.

Involvement of the brain is a rare complication and is usually preceded by similar involvement of the liver or of the lungs or both. To date not less than 62 cases of abscess of brain have been reported. Among them involvement of brain without evidence of involvement of liver or lungs are not more than five. Of the latter two were reported by Kartulis (*loc. cit.*), a third by Putney and Baker (1938), a fourth by

Stein and Kazan (1942) and a fifth by Halpert and Ashley (1944). One more is added to this from the following record.

Case report

A 60-year-old man was admitted to the Christian Medical College Hospital, Vellore, on 24th June, 1949, with a history of œdema of the legs and distension of the abdomen lasting 45 days. Breathlessness and diarrhœa for one month with blood and mucus in stools. Occasional fever with chills.

On admission he had ascites, soft pitting œdema of both legs, pallor, emaciation, well-marked clubbing of fingers. Pulse rate 80/m., regular. Heart not enlarged, no murmur. Blood pressure 95/60. Lungs: impaired resonance at both bases with diminished air entry. Nervous system: cranial nerves nothing abnormal, sensations normal, motor power normal, reflexes normal, abdominals difficult to elicit and plantar response flexor.

Laboratory examination.—Hb., 6.25 gm. W.B.C. 5,100 per cubic millimetre with a differential count of 84 per cent polymorphs and 16 per cent lymphocytes. Stool showed R.B.C. and pus cells in plenty with macrophages, no E.H. or E.H. cysts. Urine was of alkaline reaction; specific gravity 1025, albumin found in trace and deposits showed R.B.C., pus cells and granular casts. With sulphaguanidine the diarrhœa improved.

Paracentesis of the abdomen done on 28th of June and 5½ pints of straw-coloured fluid removed, the albumin content of the fluid being 0.35 per cent with a few lymphocytes and polymorphs. With a diet rich in milk his general condition seemed to improve.

On the 5th July at 11.30 a.m. the patient developed an attack of Jacksonian epilepsy. He cried out hysterically just before the attack, then the fit started with twitching of the face muscles followed by conjugate deviation of the eyes to the right and frothing at the mouth.

The fits followed one after the other at fairly frequent intervals till 6 p.m. when they appeared to be controlled. The next day he appeared somewhat stuporose. On 7th he had another attack of Jacksonian epilepsy. Thereafter he remained in a state of coma until the 14th July when he died of pulmonary œdema.

Examination following the initial attack of fits showed left pupil larger than the right and not responding to light; right pupil showed sluggish reaction. Ocular media were not quite clearly seen due to sclerosis of the lens. No papillo-œdema made out. There were arteriosclerotic changes but no hæmorrhages or exudates. Deep reflexes all over were exaggerated, plantar flexor; Kernig's absent. Roentgenographic examination of skull revealed no abnormality. Blood urea was 45 mg. and blood sugar 82 mg. per cent.

Autopsy findings: (1) *Alimentary canal*.—The peritoneal cavity contained one pint of clear straw-coloured fluid. The colon was very much thickened. The mucous membrane of the cæcum and colon showed many flask-shaped ulcers with neerotic base and typical 'dark hair' appearance. The edges of the ulcers were necrosed and covered by exudate, due to secondary infection.

Microscopically, the ulcers showed necrosis of the submucosa, and sometimes of the muscularis, with mononuclear infiltration. This picture was altered in many ulcers, due to secondary infection. Here, the surface layers and the area around the ulcers showed fibrinous exudate with polymorph infiltration. Amœbæ were found in the base and sides of ulcers.

(2) *Liver*.—The liver was slightly smaller in size, light brown in colour, coarsely granular and firm. It weighed 750 gm.

Microscopic appearance was that of the portal type of cirrhosis. The whole liver was sliced into thin pieces and no evidence of amœbic abscess found.

(3) *Spleen*.—Was slightly enlarged and covered by fibrinous deposit. The capsule was thick and consistency firm. It weighed 300 gm.

Microscopically, there was increase in the fibrous trabeculae and atrophy of the lymph follicles.

(4) *Respiratory system*.—Both the pleural spaces were obliterated by moderately firm fibrous adhesions.

The lungs showed basal œdema with emphysema of the remaining portions. There was no evidence of amœbic abscess.

(5) *Heart*.—Foramen ovale not patent.

(6) *Brain*.—There was an area of hæmorrhage and softening in the lower part of the left frontal lobe about 5 cm. in diameter. The affected part was gelatinous—the typical 'red currant jelly' appearance (figure 1, plate XLII).

Microscopically, there was hæmorrhage and necrosis with amœbæ at the edge (figure 2, plate XLII).

Discussion

The route by which *E. histolytica* reaches the brain is by no means clear, particularly in those rare instances where, as in the case reported here, the liver and lungs are not involved. It has been claimed that amœba can pass through the capillaries of the liver and lung and reach the brain. Further, a healed lesion in the liver with a subsequent lesion in the brain without involvement of the lung has been considered by some as a possibility. There is some difficulty in comprehending how the amœba can pass through the capillaries in the liver and lungs without being arrested in them. The more probable route which it takes from the intestines to brain is the one suggested by Stein and Kazan (*loc. cit.*),

the vertebral system of veins which has been demonstrated by Batson (1940). This mechanism of spread makes it easier to understand how these rare complications of intestinal amœbiasis can occur.

Collis (1944) in exhaustive review of all the theories on the pathogenesis of metastatic brain abscess from thoracic disease came to the conclusion that the method of spread is a retrograde passage of infected material from the thoracic wall to the paravertebral plexus of veins and thence to the cerebrum. He further demonstrated how the reversal of flow in the spinal system of veins is facilitated by the patient lying flat on his back.

More interesting however is Batson's demonstration how by coughing and sneezing with consequent changes in pressure inside the abdomen blood may be squeezed from the intra-abdominal veins into the vertebral system of veins. It is therefore possible that paravertebral plexus of veins may be the source of spread to the brain in the rare cases of isolated metastatic brain abscess complicating amœbic dysentery.

My thanks are due to the Pathology Department of the Christian Medical College Hospital, Vellore, and particularly to Dr. M. Asirvatham who has been kind enough to provide me with the post-mortem report and the photographs.

I am specially indebted to Dr. P. Kutumbiah, M.D., M.B.C.P., for the stimulus and direction in preparing this article.

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MADURA FOOT (MYCETOMA)

By L. M. GHOSH

N. C. DEY

and

D. PANJA

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Early history.—As a separate clinical entity, Madura foot or Mycetoma has been recognized in India since ancient times. Mention of this disease is found in the very old treatise, Atharva

Veda, in which it is described as *padavalmicum* (anthill), a condition where the foot is swollen and a kind of fleshy tumour develops on it accompanied by the discharge of a peculiar fluid. In South India the disease is endemic in and around the Madura district and has been recognized as such for a very long time. As far back as 1714, the French Missionaries at Pondicherry recognized and mentioned this condition (Collas, 1861, 1883).

Recent history.—Gill (1842) of Madura called attention to this peculiar disease of the foot which seemed to him as a distinct clinical entity. Colebrook (1844), who succeeded Gill in Madura Clinic, described the disease as Madura foot which was the name current in that part of India for a very long time. Garrison Surgeon Godfrey (1846) was the first to mention the black granules of the character of coal fragments in the diseased tissue of the foot but he ignored these granules and mentioned the condition as 'Morbus tuberculosis pedis'. Rustomji (1860) differentiated the two forms of the granules, the black and the yellow, and described what he thought the two clinical varieties of the disease. Eyre (1860) published a review on the subject. Carter (1860) recognized the fungal nature of the disease and introduced the name Mycetoma or fungus tumour. He also recognized the two clinical varieties of the disease—the melanoid or black and ochroid or yellow or white from the colour of the granules in the discharges from the sinuses. His monograph published in 1874 contains a comprehensive description of the disease. Later he pointed out the similarity of the organisms found in the Actinomycosis and in Mycetoma. Kanthak (1893) expressed the view that the black granules are only a degenerated stage of the yellow variety and both the black and yellow granules belong to the same fungus—this statement however was not confirmed by Unna. Bocarro (1893) differentiated the two varieties. Boyce and Surveyor (1894) finally established that the organisms of the black and yellow varieties are dissimilar and created the two divisions of the disease the Actinomycosis and Madura-mycosis which have since been accepted. Vincent (1894) in North Africa succeeded in culturing the fungus from the ochroid variety. Musgrave and Clegg (1907) in Philippines succeeded inoculation experiments in monkeys. Pinoy (1913) reported successful inoculation in pigeons from the culture of both varieties. Gammel (1927) and Gammel *et al.* (1926) presented a thorough review on the subject and enumerated 13 species of the genus Actinomyces and nineteen species belonging to two other classes. Ray and Tribedi (1938) published a case of mycetoma of the breast. Tribedi and Mukherjee (1939) published reports of 3 cases and included 29 other cases from the unpublished records of the pathology department of the Calcutta Medical College.

Mycetoma or Madura foot is present in all parts of the world. It has been reported from countries in Asia, Europe, Africa and America. In India it is endemic in certain parts of South India and desert areas of Central India. Castellani and Chalmers (1919) studied the epidemiology of the condition intensively. They state that the black variety is more common in the northern hot summers where the people go about barefooted. In India the black variety is more common in the desert areas of Central India and Rajputana.

Ætiology: (1) *Age.*—The disease occurs usually in adults between twenty and forty years of age when the people are of more active habits.

(2) *Sex.*—Majority of the cases are males, about 90 per cent.

(3) *Class.*—It is common amongst cultivators and field labourers who work in the fields barefooted.

(4) *Parts affected.*—In most cases the foot is the part usually affected but involvement of the trunk and upper extremities have been recorded. One of the authors (Ghosh) saw a case of Actinomyces in the navel region (unpublished). Another author (Panja) saw a case of Actinomyces jaw in an adult female (unpublished).

(5) *Exciting cause.*—Trauma—mostly a thorn-prick.

(6) *Causative organisms.*—As stated before it is a fungus disease and more than one species of the fungus is responsible. Gammel (1927) has mentioned 32 species belong to two classes and covering nine genera of which genus Actinomyces contains 13 species.

For the classification of clinical study Castellani and Chalmers classify these fungi according to the colour of the granules—(a) melanoid, (b) ochroid and (c) red.

Following Gammel, the organisms causing Mycetoma may be classified as follows:—

Mycetacea	
Class : Hypomycetes	Class : Ascomycetes
Genera : Actinomyces	Genera : Allescheria
Madurella	Aspergillus
Indiella	Sterigmatocystis
Glenospora	Penicillium
Scedosporium	

It is doubtful whether the organisms in the class Ascomycetes produce true mycetoma—the infection is mostly secondary to some other lesions and happens to contaminate the wound accidentally.

Of the five genera in the class Hypomycetes, the first three have been proved to be definitely pathogenic and for the last two a definite proof of pathogenicity has not yet been produced.

The difference between actinomyces and other genera is not difficult to recognize. The genus Actinomyces is characterized by fine mycelia,

one micron or less in diameter, with dichotomous branching and with no definite or specialized end-organs.

Mycetoma is rare in Bengal. References to its occurrence in this province are few. The notes of two cases are given below. Both patients come from the same district, belong to the cultivating class, and are in the habit of walking barefooted.

Case 1

Male, aged 46 years. Duration of illness: 2 years. Place of residence: district Howrah, West Bengal. Part affected: left foot.

History.—Started as a hard nodule on the dorsum of the foot near the second metatarsophalangeal joint. Gradually the nodule softened, suppurated and whitish granules came out with the discharge (figure 1, plate XLII). Then other nodules appeared and the lesions extended to the anterior part of the foot affecting the instep and the anterior part of the sole of the foot (figure 2, plate XLII). At present there are many nodules and sinuses from which granules come out at intervals with the discharge.

General health of the patient is good. He is not definite about the history of trauma of thorn-prick.

Skiagram.—The skiagram of the foot did not show any bone involvement or a rarefaction of bones.

The radiologist's report: A considerable soft tissue swelling is noted at the plantar aspect of the foot. No bone involvement is seen.

Culture from the granules.—Soft whitish colonies, turning pinkish.

As the organism isolated from this case was found to be identical with the organism isolated from case 2, the full study of the fungus is detailed after the report of case 2.

Treatment.—Penicillin was given parenterally and injected locally into the sinuses. 4,500,000 International Units were given internally. There was a slight improvement in the general condition of the wounds, the secondary infection was very much less, but it did not affect the original condition.

Case 2

Male, aged 38. Duration $2\frac{1}{2}$ years. Part affected: right foot. Place of residence: district Howrah, West Bengal.

The posterior and middle third of the foot including the ankle joint was affected. The lesion in this case was extensive. There was great swelling of the foot with multiple sinuses and the contour of the foot was round. There was destruction of the bones of the foot which is rather unusual.

The report of the radiologist stated that the skiagram showed evidence of extensive destruction of the small bones of the ankle joint. The talonavicular joint is obliterated. Some evidence of infection is seen on the lower end of the tibia and fibula. Madura foot with secondary infection (figures 3 and 4, plate XLII).

Evidence of bone involvement is not characteristic of Madura foot, rather the majority of observers state against the bone injury.

Though both the cases presented identical organisms, the lesions differed considerably from each other.

Conservative treatment in both the cases was unsatisfactory. Penicillin had no effect; streptomycin was not available.

The growth and character of the organisms isolated are detailed below. The organisms isolated from both the cases being identical, the study of one of them is given below.

Primary culture.—At 22°C.: no growth. 37°C.: growth in 5 to 7 days, slow growth. Anaerobic condition at 37°C.—stab culture in glucose agar: no growth.

Partial anaerobic condition at 37°C:

Blood agar growth	.. ++
Sabouraud's agar growth	.. ++
Glucose agar growth	.. ++

Aerobic condition at 37°C.:

Blood agar growth	.. +++
Glucose agar growth slow	.. +
Sabouraud's agar growth	very slow .. +
Glycerine agar	.. No growth
Glucose broth	.. No growth
Nutrient broth	.. No growth

Character of growth: Small pin-head sized colonies, whitish or cream coloured on the surface of the medium. Growth better on the dry part of the medium.

Subculture.—Sabouraud's agar: Growth slow, colonies raised, dry, wrinkled, colour whitish to cream at first, gradually becoming pink or orange.

Glucose agar: Growth +++, colour pink to orange red. Colour developed as the culture grew old. Colour more marked than in Sabouraud's medium.

Blood agar: Growth ++, colonies soft, slightly raised and slightly haemolytic.

Dorset's agar: Growth slow +, colour poorly developed.

Inspissated serum: Growth slow +.

Sugar fermentation: No fermentation.



Fig. 1.



Fig. 2



Fig. 1



Fig. 2.



Fig. 3.

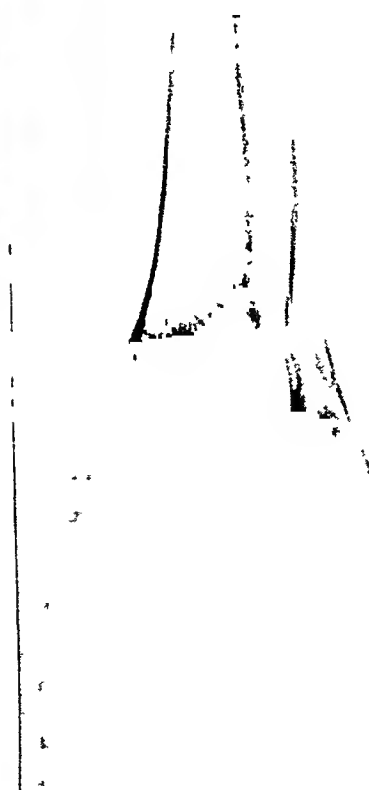


Fig. 4.

Hæmolysis : Slight and slow. Proteolysis : nil.

Milk : No clotting, becomes clear and peptonized.

Morphology : Fine mycelia less than 1 micron in diameter, branching dichotomous.

Staining characters : Gram-positive. Not acid fast.

Animal experiment.—Non-pathogenic to guinea-pigs (intraperitoneal injections).

Identity : Actinomyces Madura (Vincent, 1894).

N.B.—One specimen was sent to Professor J. T. Duncan of the London School of Tropical Medicine and Hygiene who was good enough to study it and confirm our findings.

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TREATMENT OF KALA-AZAR WITH METHYL GLUCAMINE ANTIMONIATE

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METHYL glucamine antimoniate or antimoniate of N. methyl glucamine (R.P. 2168) is a pentavalent antimony compound with the formula $SbO_3H, C_7H_{15}O_2N$, containing 28.35 per cent of antimony. The compound makes a stable watery solution and is supplied in ampoules as a 30 per cent solution. Methyl glucamine antimoniate (MGA) is reported to be of a very low toxicity, the m.l.d. being 30 mg. per 20 gm. white mouse or about 1.5 gm. per kilo. It was found to possess curative action in experimental leishmaniasis in spermo-phils and in canine visceral leishmaniasis. Sohier, Pellerat and Girard (1946) were the first to try this drug in the treatment of a case of Mediterranean kala-azar and they reported success. Subsequently other workers in the Mediterranean area reported recovery from kala-azar following treatment with MGA. Sarrouy et al. (1946) treated a child aged 5½ years, Durand et al. (1946) treated 6 cases, Sarrouy et al. (1947) 3 cases, Sarrouy et al. (1947a) 2 cases, d'Eshougues et al. (1948) an adult case and Leonardi and Pinna (1949) also an adult case of Mediterranean kala-azar with satisfactory results. One of the cases reported by Sarrouy et al. (1947a) had tuberculous disease as well and this case went on to a fatal termination. de Sousa and de Almeida (1949) treated a case of antimony-resistant kala-azar with MGA, but within a week there was a marked worsening of the condition of the patient and this drug had to be given up in favour of diamidino diphenoxy pentane that ultimately led to the cure of kala-azar.

The drug was first made available to the writer by Dr. Lucien Brumpt of Paris about the end of 1947. Since then supplies have been obtained from England and it has been possible to complete the treatment of a series of cases of kala-azar with methyl glucamine antimoniate. In this paper it is proposed to report and discuss the results of this therapeutic trial.

The drug was used for the treatment of two groups of patients under the care of the writer. A group of 19 patients (Group A) was admitted into the hospital and a small number of patients (Group B: comprising of 5 patients only who could complete the treatment, the supply of the drug running short) was treated at the kala-azar out-patients' department of the School of Tropical Medicine, Calcutta. The data relating to the first group of patients will be considered in detail and the results of treatment of the five out-patients discussed briefly, separately.

Group A: the cases admitted into the hospital

The 19 patients admitted into the hospital were all Indians, ages varying between 6 and 46 years. Fifteen were males and 4 females. Five were 'resistant' cases of kala-azar who had relapsed after one or more courses of antimonials or aromatic diamidines and the rest were ordinary or previously untreated cases of kala-azar. Protocol I gives a summary of the important clinical data relating to the 19 cases and table I an analysis of the data in the protocol I.

The diagnosis of kala-azar was confirmed in 18 cases by Napier's aldehyde test and/or the complement-fixation test for kala-azar carried out according to the technique described by the writer (Sen Gupta, 1945). *Leishmania donovani* was demonstrated in 17 cases by spleen, sternum or tibia puncture. In two patients one with cancerum oris and the other very ill showing profound leucopenia, the treatment was commenced straightway without doing any spleen or sternum puncture.

On analysis of the hæmatological findings, it is found that in 5 cases the hæmoglobin content of blood was below 6 gm. per 100 cc. of blood. These patients were very markedly anæmic and one of them had grave anæmia with hæmoglobin value of 4.2 gm. per 100 cc. All the patients had hæmoglobin values below 9 gm. per 100 cc. Fifteen patients had leucocyte counts below 4,000 per c.mm. and in one of the cases the WBC count was 700 per c.mm. with 42 per cent neutrophils.

The complications seen in this series of cases were: malaria (cases 1 and 8), cancerum oris (case 12), well-marked oedema (cases 1, 3 and 16), helminthic infection of the intestinal tract with ascaris, hookworm or trichuris (cases 2, 4, 5, 6, 8, 9, 10, 11 and 14), amœbiasis (cases 11 and 14). Severe diarrhoea, bleeding from the gums and bronchitis were the other complications noted. One of the patients had old healed foci of tuberculous infection in the upper zone of both lungs.

Treatment

Methyl glucamine antimoniate was the only drug used for the specific treatment of kala-azar after admission into the hospital. One

patient had three injections of aminostiburea at the out-patients' department previous to the admission into the hospital for the onset of cancerum oris.

The dosage was varied in different cases. The maximum single dose for an adult was 15 cc. and that for a young child 5 to 7.5 cc. and that for older children 10 cc. The injections were given by the intramuscular route and were well tolerated. In one case the total of 15 cc. was distributed in two equal amounts and injected into the two thighs each day. No serious complications ascribable to the drug were encountered. One of the patients had epileptiform convulsions during the course of injections but this patient had previous history of epilepsy.

The total dose of the drug for the patients who responded to treatment varied from 87.5 to 215 cc. with the mean at 165.6 cc. for adults and from 82.5 to 145 cc., mean 113.0 cc., in children. The mean relative total dose per 100 lb. body weight was 181.36 cc. for adults and 319.8 cc. for children.

Subsidiary treatment for anæmia and the treatment of coexisting infections and complications were carried out following the scheme described by the writer elsewhere (Sen Gupta, 1949).

Results of treatment

All the fourteen ordinary cases and the three resistant cases of kala-azar showed signs of recovery following the treatment with methyl glucamine antimoniate. In two resistant cases the drug proved unsuccessful.

In the cases that recovered the fever subsided after 2 to 6 injections in 9 cases, after 6 to 12 injections in 4 cases and at the end of the course of injections in 3 cases. One case was afebrile throughout. The serious complications responded to appropriate treatment and there was marked improvement of general health. On examination during convalescence after the completion of treatment of kala-azar and its complications, 16 of the 17 patients who recovered showed distinct gain in weight. One patient showed slight loss of weight; this might have been due to the loss of oedema. There was well-marked general and hæmatological improvement in this case at the end of treatment. There was well-marked shrinkage of the spleen, pronounced improvement of the leucocyte count and hæmoglobin level of blood in the cases that recovered (see protocol I and table I). All the cases were discharged as apparently cured.

In 2 resistant cases the drug proved unsuccessful. Brief notes of these 2 cases are given below. Fuller accounts of these extremely drug-resistant cases are expected to be published later.

Case 18.—An Indian boy from upper Assam, aged 9 years, was admitted for kala-azar in January 1948. The onset was enteric-like and the diagnosis of kala-azar was made during recurrence of pyrexia after the

PROTOCOL

Summary of the case notes of the patients

Serial number	1	2	3	4	5 R.	6	7
Age in years	16	6	16	10	32	23	30
Sex	m.	f.	m.	m.	m.	m.	m.
Weight in lb.	56	28	60	46	74	90	84
Duration of illness (months)	8 (?)	(?)	12	7	7	2	6
Spleen, inches, below costal margin	P.	3	5	2	4	3	2
Hæmoglobin, gm. per cent	8.7	..	8.25	8.9	8.52	4.26	8.9
Leucocytes, $\times 10^3$ /c.mm.	2.5	4.6	4.0	4.2	2.4	0.7	3.4
Aldehyde test	(-)	-	+++	+	+++	..	+++
Complement fixation test	..	++	++	++	++	++	++
L.-D. bodies	+	++	+	+++	+	..	++
Total dose of MGA (cc.)	87.5	87.5	95	82.5	210	215	210
Total dose per 100 lb. body weight (cc.)	156.2	312.5	158.3	179.3	283.7	238.8	250
Maximum single dose (cc.)	10	10	10	10	15	15	15
Number of injections	10	12	10	10	9	15	15
Fever subsided after number of injections	4	12	10	5	9	3	0
Days after treatment	25	30	21	11	22	13	14
Hæmoglobin, gm. per cent	12.4	10.3	9.6	8.9	9.6	9.9	11.275
Leucocytes, $\times 10^3$ /c.mm.	9.2	8.75	10.2	6.9	4.25	6.4	7.0
Spleen, inches, below costal margin	0	0	3	P.
Weight in lb.	64	34	70	58	82	98	91
Immediate result	C.	C.	C.	C.	C.	C.	C.
Final result	C.	C.

Abbreviations.—R. = resistant case; m. = male; f. = female; St. = sternum puncture; under the costal margin; C. = cure; F. = failure;

with hydroxystilbamidine, neostibosan and stilbamidine. The case is still under observation.

Case 19.—Young man, aged 23 years, an indigenous case of kala-azar from Bombay City from which a few cases have been reported during the recent years, was admitted for kala-azar since June 1947. Diagnosed as kala-azar in 1948 and treated successively with carbostibamide 2.725 gm., carbostibamide 1.2 gm., neostibene six injections (? total dose), urea stibamine 1 gm. in 5 injections. The first 3 courses of injections were followed by relief for 2 months, 1 month, and 6 weeks respectively. The last course of injections led to a slight lowering of temperature but no improvement of general health. Admitted into the Hospital for Tropical Diseases in 1949. On admission the patient showed copious albumin, hyaline and granular casts, and degenerated leucocytes in the urine besides signs of advanced kala-azar.

He was treated with 30 injections of hydroxystilbamidine, total dose 4.45 gm., and was discharged apparently cured, there being marked improvement of general health, and the blood picture; the spleen had shrunk considerably and the urine showed only traces of albumin and no casts or pus cells. Two months later there was a relapse of kala-azar. The patient was re-admitted and treated with 15 injections of MGA, total dose 210 cc., the injections being given on alternate days. There was a remission of fever at the end of the course of injections but the fever recurred within a week of completion of treatment, and there was no improvement of general health. The patient was soon very ill with high fever and the urine again showed copious albumin, and granular and hyaline casts. The patient was treated symptomatically and on the fever coming down to a lower level and the urine showing improvement, he was given two courses of injections of stilbamidine (total 30 injections) and was discharged as apparently cured having fulfilled all the criteria of immediate cure, viz, afebrile, gain in weight by 12 lb., hæmoglobin 15.5 gm. per 100 cc., leucocytes 7.2 thousand, spleen just palpable.

Relapses

Eleven of the 17 patients, discharged as apparently cured, were either seen or replied to the follow-up circular more than six months after the completion of treatment. Ten of these patients were either found to be in good health or replied stating that they were in good health, free from all symptoms or signs of kala-azar. One of the patients replied stating that there was a relapse for which further specific treatment had been necessary (case 9).

Group B : the cases treated at the out-patients' department

Five patients were treated with MGA at the out-patients' department. The diagnosis was confirmed in four of these cases by Napier's aldehyde test (+++ or ++) and by finding the leishmania in the ileum puncture smear in the fifth case. Two were children aged 4 and 6 years, and 3 adults aged 16, 32 and 35 years. The injections of MGA were given twice a week and the maximum single dose was 5 cc. for children and 15 cc. for adults. The number of injections varied from 7 to 13. The total doses for the 5 cases were 63 and 55 cc. for the children and 90, 155 and 105 cc. for the adults. In all the five cases, the fever subsided and there was marked improvement of general health and reduction of splenic enlargement. Blood count was done in 3 of the cases after the completion of specific and the necessary subsidiary treatment. There was marked improvement of leucocyte count

I

treated with methyl glucamine antimoniate

8 - 9 R.	10	11 R.	12	13	14	15	16	17	18 R.	19 R.	
6 f. 30 (?) 2 8.52 3.75 .. ++ +	8 f. 34 19 6 6.875 1.9 +++ ++ ++	17 m. 81 2 4 1/2 7.56 2.3 +++ ++ +	40 m. 126 9 5 1/2 8.25 3.0 + + Spl.	11 m. 46 2 4 6.8 2.9 ± ++ ..	46 m. 101 7 5 8.25 4.3 +++ ++ +++	25 m. 100 1/2 4 8 1/2 6.8 2.85 +++ + +	17 m. 84 6 4 1/2 8.25 1.7 +++ A.C. +++	16 f. 71 1/2 4 2 1/2 8.25 1.4 +++ A.C. +++	28 m. 91 4 4 1/2 6.18 1.9 ± ++ +	9 m. 42 22 7 7.15 2.5 ± + +	23 m. 107 54 5 8.8 0.85 ± + +++
Tibia.	Spl.	St.	Spl.	Spl.	Spl.	Spl.	St.	St.	Spl.	Spl.	
145	105	210	165	145	155	170	165	155	150	45	
483	308.8	259.2	130.9	315.2	153.4	168.0	196.4	216.6	164.8	100	
10	10	15	15	10	15	15	15	15	15	7.5	
15	11	15	13	15	11	12	11	11	11	8	
15	8	2	5	15	2	6	5	12	2	No effect	
15	31	7	5	30	6	..	13	64	4	1	
12.375	9.9	11.68	11.68	9.86	8.25	..	11.275	13.75	11.0	5.5	
13.4	9.8	8.4	6.0	4.1	6.4	..	12.9	7.9	5.8	1.15	
1 r.	3 r.	< 1 r.	1 r.	2	3	..	P.	0	0	6 1/2	
28	43	91	129	48	110	105	85	++	98	40	
C.	C.	C.	C.	C.	C.	C.	C.	C.	C.	F.	
Relapse	C.	C.	C.	C.	C.	..	C.	C.	C.	X	

Spl. = spleen puncture; Tibia. = tibia puncture; r. = mobile and replaceable
A.C. = serum anti-complementary; P. = just palpable.

and haemoglobin in all the cases. The adult patient who had only 7 injections showed remarkable response. She had marked degree of macrocytic anaemia (Hb. 6 gm. per 100 mil., MCV 123.0 cu. μ), and splenic enlargement to 7 inches below the costal margin. Two weeks after the completion of the specific treatment, the spleen was just palpable though marked anaemia persisted. She was next given injections of whole liver extract (4 cc. \times 6). The next blood count showed the haemoglobin value as 12 gm. per 100 mil., leucocytes 7,000 per c.mm. and the patient showed marked improvement of health.

It was apparent that immediate clinical cures could be achieved by giving the injections of MGA twice a week. The treatment of these 5 cases was finished less than 6 months ago. Thus it is not yet possible to establish whether the cures were permanent.

Discussion

On consideration of the results of treatment of kala-azar with methyl glucamine antimoniate, it will be apparent that this drug possesses considerable anti-kala-azar activity. Immediate clinical cures followed in 22 out of the total of 24 cases treated by the writer in the hospital and the out-patients' department. The writers from the Mediterranean countries also reported excellent immediate results.

The 2 cases in which the drug failed to effect a cure were extremely drug resistant and had

relapsed after repeated courses of injections of antimonials and diamidines. It is yet unknown if any drug or combination of drugs will lead to the cure of these 2 cases or whether it will be necessary to resort to splenectomy and further chemotherapy. It is more correct to state that immediate clinical cures resulted in all the 19 ordinary cases and in 3 out of 5 resistant cases.

It is however well known that the immediate clinical cure rate does not always indicate the true therapeutic value of an anti-kala-azar drug. Excellent immediate results may be obtained but there may occur relapses in a high proportion of the cases later on (cf. Napier and Sen Gupta, 1943; Sen Gupta, 1944; Sen Gupta, 1945a; Sen Gupta and Chakravarty, 1946; Sen Gupta, 1948). In order that a drug may be regarded as satisfactory, the relapse rate must be reasonably low.

It has been pointed out by Napier and his co-workers that about 95 per cent of the cases of Indian kala-azar that are going to relapse do so within four months and practically all within 6 months. So if a patient remains free from all symptoms of kala-azar for six months after specific treatment, he may for all practical purposes be regarded as permanently cured.

Of the 17 patients discharged from the hospital as cured, 11 patients could be followed up six months or more after the completion of treatment. Ten patients were free from

all symptoms of kala-azar and were thus in all probability permanently cured. One ordinary case of kala-azar relapsed and had further treatment. It may thus be agreed that the relapse rate is not very high (1 in 11 cases)*.

The variation of the total dosage in different cases was adopted to find out an average curative dose of the drug. It has been found that the mean total dose per 100 lb. body weight for the cases that were cured was 181.36 cc. for adults and 319.8 cc. for children. This illustrates the well-known fact that children require relatively larger total doses of antimonials for the treatment of kala-azar. The total dose may be roughly calculated as 2 cc. per pound body weight for adults with the total not exceeding 225 cc. and 3 cc. per lb. body weight for children. Following the scheme adopted in this therapeutic trial, the total dose should be given in 14 or 15 injections given intramuscularly on alternate days. The initial dose should be 5 cc. for an adult and 2 or 3 cc. for a child. It is preferable not to exceed 15 cc. as maximum single dose for an Indian adult and for children the maximum single dose should be between 5 and 10 cc. according to the age and weight of the patient. From the experience of treatment of the small number of cases at the out-patients' department, it appears that the drug is effective even when given twice a week.

On consideration of the antimony content of methyl glucamine antimoniate, it would seem that the amount of antimony administered is well above the margin of safety (cf. Reviewer, *Trop. Dis. Bulletin*, 1947, **44**, 56). As already indicated methyl glucamine antimoniate contains 28.35 per cent of antimony and the 30 per cent solution contains 0.425 gm. of Sb. in 5 cc. Hence if we administer 15 or even 20 cc. as single doses, the amount of antimony administered per dose will be 1.275 to 1.7 gm. On comparison with the older antimonials such doses would appear to be very high and dangerous. But it has to be pointed out that MGA is a drug with a very low toxicity. The minimum lethal dose of MGA is 1.5 gm. per kilo; that of urea stibamine lies between 0.220 and 0.250 gm. per kilo. Also the drug is rapidly excreted. In healthy subjects all traces of antimony disappear from the urine 24 hours after the administration of MGA, and in kala-azar patients traces of Sb. could be detected till 36 hours but not after 48 hours (Durand *et al.*, *loc. cit.*). Thus doses of 1.275 to 1.7 gm. of MGA can be safely administered as single doses every 48 hours to individuals weighing 50 or 60 kilo, because each single dose is less than 1/50 of the minimum lethal dose for an individual of the same weight. This may be

contrasted with the dosage of urea stibamine of which the largest single dose generally used for an adult weighing about 50 or 60 kilo, viz 0.20 gm., is similarly less than 1/50 of the m.l.d.

Summary

1. A series of 24 cases of kala-azar was treated with methyl glucamine antimoniate (R.P. 2168). The drug was administered by intramuscular injections on alternate days in most of the cases. The mean total dose per 100 lb. body weight was 181.36 cc. of the 30 per cent solution corresponding to 15.4 gm. of antimony for adults and 319.8 cc. per 100 lb. body weight for children corresponding to approximately 3 cc. per pound body weight. The injections were well tolerated.

2. Nineteen ordinary, i.e. previously untreated cases, and 3 antimony-resistant cases recovered and the drug proved unsuccessful in 2 extremely drug-resistant cases.

3. On following up the cases 6 months after their immediate clinical cure 1 case out of the 11 that could be contacted showed relapse. The relapse rate was thus not very high.

4. An average effective total dose of methyl glucamine antimoniate for the treatment of Indian kala-azar has been worked out.

The writer is thankful to Dr. L. Brumpt and The Specia (Societe Parisienne D'Expansion Chimique, S.A.) and to Messrs. May and Baker, Ltd., Dagenham, England, for the free supplies of methyl glucamine antimoniate, viz, Glucantime (Specia) and Protostib (M&B), for clinical trial.

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*In a recent follow-up over six months after treatment with aminostiburea at the kala-azar outpatients' department, there was a relapse of kala-azar in 2 cases out of 25 (P. C. S. G.).

LABORATORY DIAGNOSIS OF SCRUB TYPHUS

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THE diagnosis of typhus fever is confirmed by animal inoculation and Weil-Felix test. The result of 17 cases thus examined is reported.

As to the animal inoculation method through-out Haffkine's strain of white mice is used. 1 cc. of patient's blood taken in equal volume of sterile 3.8 per cent citrate saline is sent to the laboratory. It is centrifugalized, the supernatant fluid is discarded, another change of saline put in, mixed and centrifuged again. This is repeated in all three times, finally the supernatant fluid is thrown away leaving the cells only.

These cells are injected intraperitoneally into the white mouse. In a typical case the animal becomes ill between the 6th and the 12th day, a common feature is the standing up of hair and not taking food readily. As a rule on the 8th day of inoculation the animal is killed by

chloroforming and the abdomen opened. In a typical case a sticky blood-stained fluid is seen in the peritoneal cavity, well demonstrated by placing the flat side of the scalpel on the loops of bowels and raising it when stringy strands are noticed. The spleen is appreciably enlarged and the intestinal loops look shrivelled up and bile-stained.

Smears from the peritoneal fluid and scrapings from the parietal peritoneum are taken. These are stained with 1 in 50 diluted Giemsa 2 drops in 3 cc. of diluted Leishman, after fixation in alcohol, allowed to stand for 15 minutes, washed in tap water, dried and examined. The rickettsia bodies are typically seen in groups intracellular in the cytoplasm of endothelial cells.

The findings in the 17 cases thus investigated are shown in two tables. Table I shows the number of cases where *Rickettsia orientalis* has been demonstrated by animal inoculation and table II shows the remaining cases where only Weil-Felix was positive.

TABLE I

Details of 10 positive cases by animal inoculation method

Serial number	Duration of fever	WEIL-FELIX			Date when Weil-Felix done	Animal inoculated Opened on
		ONK	OX19	OX2		
1	13th day	125	22-9-49	{ 16-9-49 24-9-49
2	16th day	{	{	{	{ 20-9-49 26-9-49 27-9-49	{ 27-9-49 5-10-49
3	10th day	{ .. 250 ..	{	{	{ 27-9-49 1-10-49 6-10-49	{ 1-10-49 9-10-49
4	10th day	{	{	{	{ 12-10-49 14-10-49 18-10-49	{ 15-10-49 22-10-49
5	4th day	25-10-49	{ 25-10-49 2-11-49
6	6th day	28-10-49	{ 28-10-49 5-11-49
7	15th day	{ .. 625 ..	{ .. 125 ..	{	{ 25-10-49 27-10-49 2-11-49	{ 2-11-49 10-11-49
8	2nd day	{ 125 1,250 ..	{	{	{ 7-11-49 12-11-49 16-11-49	{ 12-11-49 20-11-49
9	4th day	{ .. 250 ..	{	{	{ 14-11-49 18-11-49 28-11-49	{ 18-11-49 26-11-49
10	5th day	{ 125 125 ..	{	{	{ 19-11-49 26-11-49 30-11-49	{ 19-11-49 28-11-49

TABLE II
(Weil-Felix positive and animal inoculation negative)

Serial number	Duration of fever	WEIL-FELIX			Date when Weil-Felix done	Animal inoculated Opened on
		OXK	OX19	OX2		
1	13th day	625	21-9-49	{ 22-9-49 30-9-49
2	10th day	1,250	20-9-49	{ 22-9-49 30-9-49
3	14th day	{ 125 250	{ 1-10-49 6-10-49 11-10-49	{ 1-10-49 9-10-49
4	11th day	{ 625	{ 11-10-49 19-10-49	{ 11-10-49 19-10-49
5	48 hours	125	15-10-49	{ 15-10-49 23-10-49
6	11th day	{ 125	{ 19-11-49 22-10-49	{ 22-10-49 30-10-49
7	10th day	{ 625	{ 15-11-49 17-11-49 22-11-49 26-11-49	{ 17-11-49 25-11-49

Summary and conclusions

Attempt has been made to study 17 cases to find out the value of animal inoculation method combined with Weil-Felix reaction. In four cases where Weil-Felix turned out negative on three successive occasions the animal inoculation method proved positive (table I, nos. 2, 4, 5 and 6). In four other cases, *i.e.* table I, nos 1, 3, 9 and 10, the animal inoculation method showed rickettsia bodies before the appearance of Weil-Felix in a diagnostic titre. In cases, table I, nos. 7 and 8, the animal inoculation test turned out positive along with Weil-Felix positive in a titre of 625 and 1,250 respectively. - Thus in 8 out of 17 cases investigated the animal inoculation test proved to be helpful either earlier than Weil-Felix or about the same time as that of Weil-Felix. Altogether 10 out of 17 cases showed rickettsia bodies, *i.e.* in 58 per cent of the cases. From this it can be inferred that animal inoculation method particularly in the early stages of typhus fever is of definite value and if coupled with Weil-Felix reaction it is possible to diagnose practically all cases of scrub typhus which is the type prevalent in Jamshedpur.

In table II there are seven cases showing Weil-Felix positive and all negative to animal inoculation. With the exception of case no. 5, which was sent pretty early, all the others were sent 10 days and later. Moreover, cases nos. 5 and 6 do not show a high diagnostic agglutination titre.

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ADVENT OF ELKOSIN

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WITH a view to avoiding untoward side-effects like vomiting, giddiness and especially crystaluria, the writer tried in a few cases a new sulpha-drug recently introduced by Ciba under the name Elkosin.

The manufacturers claim that this drug, which is chemically 6-p-aminobenzenesulphonamido-2,4-dimethylpyrimidine, is far more soluble than other sulpha-derivatives, so that crystaluria is made impossible even after administration of highest therapeutic doses.

The results of a few cases treated with Elkosin are shown in the following chart.

Eleven cases of complications in measles were treated during this season, in three families.

one following the other (4 in one, 5 in one and 2 in one family). Parallel cases are grouped together, and only chief points are given to save space:—

A TABLE OF CASES OF MEASLES

Age, etc.	Details of diagnosis	Complications	Treatment	REMARKS
H., F., 2½ years, 1st day.	Fever, 101° to 102°F. or near about in almost all cases with sudden onset and typical morbilliform rash, with slight nasal discharges, cough, and in most cases temperature began 99° to 101°F., conjunctivitis and Koplik's spots present.	Acute tonsillitis in the children over 3 years.	Treatment given according to age with Elkosin, varying from ½ tablet to 1 tablet every 6 hours, 4 times a day, with other symptomatic treatment as alkali mixture, cleanliness of mouth and other hygienic measures and dietetics.	Fever came down to normal on the next day or day following. Rash: not suppressed in any case. No other complications noticed. Uneventful recovery without any symptoms such as sometimes seen in bad cases.
H., F., 4 years, 1st day.				
H., F., 6 years, 1st day.				
H., M., 3 years, 2nd day.				
H., F., 3½ years, 3rd day.				
H., M., 5 years, 1st day.				
H., M., 2⅔ year, 2nd day.				
H., M., 9 years, 3rd day.	Same as above with temperature 102° to 103°F.	Broncho-pneumonia and tonsillitis in both.	As in above: Elkosin 1 tablet 4 times a day; Alkali mixture, gargles, etc.	Temperature normal on the day following, treatment continued; weakness marked.
H., M., 6 years, 2nd day.	Ditto	Ditto	Ditto	..
H., M., 10 years, 3rd day.	Ditto	Ditto	Ditto	..
H., F., 22 years, unmarried.	Same as before, rash rather discrete.	Acute tonsillitis and bronchitis.	Elko-in 2 tablets every 4 hours, with other symptomatic treatment.	Results showed quick recovery of the patient, but menstruation was delayed for about a week (period was due when patient fell ill).
H., M., 5 years.	Temperature 101° to 102°F. every evening from first day on. Blood smear for M.P. negative. 2nd day—measly rash, not very marked. 3rd day—morbilliform rash heavy: temperature 105.4°F., blood smear for M.P. negative.	Acute broncho-pneumonia (both sides), acute laryngitis, tonsillitis, etc.	First 2 days: Elkosin ½ tablet thrice daily with other symptomatic treatment. 3rd day Elkosin 1 tablet every 4 hours, plenty of fluids and usual mixture.	Temperature came down to normal on the 4th day. Lung symptoms disappeared on the 6th day. Patient looked comfortable from the 7th day.
H., F., 20 years, married; pregnancy 8 weeks.	Measles, usual course of temperature and rash.	Acute tonsillitis and bronchitis.	Elkosin 2 tablets 4 hourly, with simple mixtures as required.	No untoward symptoms noticed. Patient was under observation for 4 weeks, after treatment. Pregnancy continued.

Elkosin was also tried in a number of abortions with complications, a case report on which is given hereunder :—

A TABLE OF CASES OF ABORTION

Age, etc.	Details of diagnosis	Complications	Treatment	REMARKS
H., F., 18 years, primipara.	Abortion : 11 weeks	Temperature 102°F., bleeding.	Evacuation under i.v. Anæsthesia (pentothal sodium). Elkosin 2 tablets every 4 hours for the 1st day. Glucose 100 cc.; Elkosin 2 tablets every 6 hours for the remain- ing three days.	..
H., F., 20 years, 3 p.	History of previous abortions : 2. 16 weeks.	Incomplete Pulse—low 110, tem- perature 99°F.	..	No temperature from the 2nd day.
H., F., 24 years.	2 abortions—one living child.	Parallel cases almost	..	Temperature remaining for a few days; unevent- ful recovery.
H., F., 25 years.	2 p. 3rd abortion.
H., F., 27 years.	One abortion—one living child.	W.R. negative	Treatment given almost same.	..
H., F., 23 years, 2 p. H., F., 28 years, 2 p. H., F., 32 years, 3 p. H., F., 36 years, 5 p. H., F., 36 years, 6 p. H., F., 38 years, 9 p. H., F., 39 years, 7 p. H., F., 40 years, 4 p.	Cases of inevitable abortion varying from 12 to 14 weeks.	..	Prophylactic with Elkosin, 2 at a time, 3 times a day: after either spontaneous expulsion after medical treatment or evacuation performed as was necessary under anæsthesia.	Uneventful. Nothing particular.
H., F., 19 years, primipara.	Incomplete abortion, evacuation done by digital manipulation under pentothal sodium.	Temperature 105°F. M.P. ++. Leucocyte count 13,000. 4th day—M.P. nil. Leucocyte count 13,500.	Antimalarial treatment given. Temperature went down to 99°F. on the 3rd day; 4th day : temperature shot up to 104°F. Antimalarial treatment given, tem- perature almost same. Elkosin given 3 tablets every 4 hours (glucose 100 cc.). Temperature came down to normal on the 6th day morning. Treatment was con- tinued for 4 more days : routine antimalarial treatment was con- tinued, though tempera- ture was normal all through afterwards.	Latter part uneventful, but patient was rather anæmic. Treatment on that line given.

A TABLE OF CASES OF ABORTION—*contd.*

Age, etc.	Details of diagnosis	Complications	Treatment	REMARKS
H., F., 40 years, 6 p.	Abortion 18 weeks	Temperature 101.5°F. M.P. negative, leucocyte count 12,350. Other conditions good.	Evacuation under general anaesthesia. Elkosin 3 tablets every 6 hours for 5 days; normal temperature from the 3rd day.	Rest of the period uneventful.
H., F., 41 years.	History of abortion (10 days before).	Temperature 102.4°F. patient anxious, M.P. negative, leucocyte count 9,500, urine culture (growth of <i>B. coli</i> scanty).	Elkosin 2 tablets every 4 hours, 4 times a day. Alkali with diuretics. Plenty of fluids as usual.	Temperature came down slowly by a degree a day, until it came down to normal on the 6th day. Treatment was continued, for 3 days more, one tablet a day 4 hourly. Uneventful recovery.

Furthermore, a few cases of puerperal fever, one case of breast abscess, a few cases of gonorrhoea and one case of chicken pox, complicated with laryngitis and bronchitis, were also treated with Elkosin. The results of treatment of these cases are given hereunder:—

A TABLE OF MISCELLANEOUS CASES

Age, etc.	Diagnosis	Complications	Treatment	REMARKS
H., F., 22 years, 2 p., normal labour.	Pp. fever	Almost parallel cases of Pp. fever with pneumonia, 2nd day.	Elkosin 2 tablets, 4 hourly, 4 times a day with additional measures as required.	Recovery during the usual course of a week. No other complications noticed.
H., F., 23 years, primipara, normal labour, perineal tear stitched.				
H., F., 22 years, unmarried.	Breast abscess, right breast.	Started as interstitial mastitis: case seen on the 4th day. Temperature 101° to 103°F. average. No fluctuation detected till then. Later fluctuation detected.	Elkosin 2 tablets, 4 hourly, 4 times a day: plain alkali mixture. Incision given: pus drained and dressed. Treatment continued for 7 days after drainage until discharge subsided; dressings continued with Cibazol powder.	Temperature came down to normal the day after drainage. Complications none of any import.
H., F., 17 years.	Gonorrhoea	Early cases	Elkosin 4 tablets, 4 hourly, on the 1st day, 4 times a day. Three tablets 4 hourly on the 2nd day; 2 tablets 4 hourly 4 times a day for the remaining 5 days to complete a course followed by diuretic mixtures.	Complications none so far: no toxic symptoms noticed.
H., F., 23 years.				
H., F., 37 years.				
H., F., 31 years.	Gonorrhoea with acute cystitis.	Ditto	Elkosin 2 tablets, 3 times a day. Treatment continued as before.	No fever from the 3rd day. A few eruptions became pustular from vesicular; rest started drying up; almost all the eruptions started forming scabs from the 5th day. Patient still under observation, to-day being 8th day (17-4-50), conditions very satisfactory.
H., M., 58 years.	Temperature 101° to 103°F., chicken pox. Discrete vesicular eruptions on the day the patient was seen. Heavy rash on the following day.	Acute laryngitis, bronchitis (mild).		

From the different groups of cases treated with Elkosin as noted above, none of the patients, from the child on to an adult, male or female, showed any toxic effects. The conclusion may safely be drawn that the treatment with this new drug can be continued for several days as found necessary without any unfavourable side-effects. It seems to the writer that Elkosin, which gave excellent results in all the above-cited cases, is definitely superior to other sulpha-drugs.

THE ANTIBACTERIAL PRINCIPLE OF THE BETEL LEAF

A PRELIMINARY REPORT

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and

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THE digestive and medicinal value of the betel leaf has been known in India for centuries. The leaves are generally used for chewing, in the form of packets (commonly called 'beeda' or 'pán') with the addition of lime, arecanut, catechu, cardamoms, nutmeg, cloves and camphor.

In treatises on Ayurveda, the betel leaf has been stated to have beneficial effects on the throat, larynx, respiratory and digestive organs, particularly in conditions like cough, dyspnoea and indigestion in children. According to Susruta, it is aromatic, carminative, stimulant and astringent. Internally it is administered in cases of snake bite (Chopra, 1933). It sweetens the breath and improves the voice. The warm leaves smeared with oil are applied to the chest as a poultice in bronchitis and coughs, in infancy and childhood (Nadkarni, 1927). In some parts of South India, poultices containing betel leaves are applied to the eruptions on the body, as in cases of smallpox. They are used as dressings for foul ulcers. The juice is dropped into the eye in ophthalmia or into the ear (warmed) to relieve earache. Internally it is administered as a febrifuge and antipyretic in children (Ghosh, 1939). The antibacterial property of the betel leaf has been studied by George, Venkataraman and Pandalai (1947).

The present investigation was conducted to study the inhibitory effect of extracts of betel leaf upon various organisms.

Technique

Experiment 1.—Fresh betel leaves were obtained from the bazaar and washed first in tap water and subsequently in distilled water. Twenty leaves weighing 30 gm. were crushed in a mortar with 30 cc. of distilled water and the juice was collected and filtered. The greenish fluid obtained was centrifuged to remove coarse particles. Dilutions (in normal saline) of 1 in 5, 10 and 20 of the supernatant liquid were made and distributed in 2 cc.

quantities in sterile test tubes; a drop (0.05 cc.) of a saline emulsion of an 18 hours' culture of *B. coli** was put into each of the tubes and incubated for 2 hours at 37°C. At the end of this period a drop of the contents of each tube was planted on Douglas agar slopes and incubated till next morning. It was found that all tubes showed a growth of *B. coli* indicating that an aqueous extract of betel leaves has no inhibitory effect on *B. coli*.

Experiment 2.—An ethereal extract of betel leaves was prepared according to the following technique. Seven leaves weighing 10 gm. were cut into small pieces and extracted with ether in a Soxhlet continuous extraction apparatus for two hours. The resulting ethereal extract was evaporated to remove ether. The residue consisted of a greenish-yellow liquid and some black semi-solid and had the characteristic odour of betel leaves. It was taken up in 7 cc. of normal saline and filtered from insoluble matter. The filtrate was sterilized by candle filtration and then tested as follows:—

Dilutions of 1 in 5, 10 and 20 (using normal saline) were made and distributed in 2 cc. quantities in sterile test tubes. One drop (0.05 cc.) of a saline suspension of an 18 hours' culture of staphylococcus (Oxford strain)* was added to each tube and incubated for 2 hours at 37°C. At the end of this period, a drop of the contents of each tube was planted on Douglas agar slopes and incubated till next morning.

Result: 1 in 5 and 10, no growth; 1 in 20, growth +; control, growth +++.

Experiment 3.—An experiment similar to no. 2 except that the following organisms were employed for the test: (1) non-haemolytic streptococcus, (2) haemolytic streptococcus, (3) pneumococcus. Dilutions of 1 in 10, 15 and 20 of the betel leaf extract were employed and the mixtures of these and the culture suspensions were incubated for 4 hours at 37°C. instead of 2 hours. The results are shown in table I.

TABLE I

Culture	GROWTH AFTER 18 HOURS			
	Dilutions			
	1 in 10	1 in 15	1 in 20	Control
Non-haemolytic streptococcus	—	++	++	+++
Haemolytic streptococcus	—	—	—	+++
Pneumococcus*	—	—	—	—

* Due probably to some technical error, the control in the case of pneumococcus did not show any growth. This experiment has been repeated (see table II).

Experiment 4.—An alcoholic extract of betel leaves was prepared as follows:—

* The opacity of the suspensions of *B. coli*, staphylococcus and other organisms employed in the experiments corresponded to no. 10 opacity tube (Brown's).

The leaves after ether extraction were extracted with dehydrated alcohol in a Soxhlet extraction apparatus for 7 hours. The resulting alcoholic extract on evaporation of the alcohol gave a light green liquid with some black viscous oil. The whole was mixed with four times its volume of water and filtered from insoluble matter. The filtrate was sterilized by candle filtration and then tested for antibacterial property against 5 organisms. The results of the test are shown in table II.

The results show that the water soluble portion of an ethereal extract is very highly potent against these organisms.

Experiment 6.—This was performed to test the heat stability of the water soluble portion of an ethereal extract of betel leaves. Some of the aqueous solution prepared in experiment 5 was heated in a boiling water bath for 1 hour and then compared with an unheated sample. The results are given in table IV.

TABLE II

Culture	Control	BETEL LEAF EXTRACT : GROWTH AFTER 18 HOURS				
		1 in 5	1 in 10	1 in 15	1 in 20	1 in 40
<i>B. typhosus</i>	+++	+++	+++	+++	+++	+++
<i>B. paratyphosus A</i>	+++	+++	+++	+++	+++	+++
<i>B. paratyphosus B</i>	+++	+++	+++	+++	+++	+++
<i>Staphylococcus</i> (Oxford strain) ..	+++	+++	+++	+++	+++	+++
<i>Pneumococcus</i>	+++	—	—	+	++	++

The results show that except in the case of pneumococcus, an alcoholic extract of the residue left after ether extraction has no inhibitory effect on the other organisms. In other words, practically all the antibacterial principle is extracted by ether.

Experiment 5.—An ethereal extract from 39 gm. of betel leaves was evaporated and dried in a vacuum desiccator. The residue was dissolved in 15 cc. water and filtered from insoluble matter. The filtrate was sterilized by filtration and then tested for antibacterial activity as follows :—

Dilutions of 1 in 10, 20, 50, 100 and 200 were made and five organisms employed for the test the results of which are recorded in table III.

The results show the antibacterial principle in an ethereal extract of betel leaves is heat stable. Further investigation is proceeding.

Summary

1. A study has been made to find out if there is an antibacterial principle in the betel leaf.
2. An aqueous extract has been found to contain no inhibitory activity against *B. coli*.
3. The water soluble portion of an ethereal extract of the betel leaf has been found to have an inhibitory effect on several organisms.
4. An alcoholic extract of the residue left after ether extraction was found to have practically no antibacterial activity. All the

TABLE III

Culture	DILUTIONS OF ETHEREAL EXTRACT OF BETEL LEAVES : GROWTH AFTER 18 HOURS					Control
	1 in 10	1 in 20	1 in 50	1 in 100	1 in 200	
<i>Pneumococcus</i>	—	—	—	—	—	+++
<i>Hæmolytic streptococcus</i>	—	—	—	—	—	+++
<i>Non-hæmolytic streptococcus</i>	—	—	—	—	—	+++
<i>Staphylococcus</i> (Oxford)	—	—	—	—	—	+++
<i>B. coli</i>	—	—	—	—	—	+++

TABLE IV

Culture	Extract	DILUTION OF EXTRACT : GROWTH AFTER 18 HOURS					Control
		1 in 100	1 in 200	1 in 400	1 in 800	1 in 1,600	
<i>B. typhosus</i> ..	{ Heated ..	—	—	—	—	—	+++
	{ Unheated ..	—	—	—	—	+++	
Staphylococcus (Oxford)	{ Heated ..	—	—	—	—	—	+++
	{ Unheated ..	—	—	—	—	+	

antibacterial principle had gone into the ether solution.

5. The antibacterial principle in the ethereal extract is heat stable and resists a temperature of 100°C. for 1 hour.

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A Mirror of Hospital Practice

REITER'S DISEASE

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REITER'S disease may be described as a syndrome of unknown aetiology presenting the classical triad of bilateral conjunctivitis, arthritis and urethritis. Ilmari Paronen of the University of Helsinki studied 344 cases on the Karelian Isthmus, originating mostly in a widespread epidemic of Flexner's dysentery, and he concludes that Reiter's syndrome occurs only after dysentery and that the dysentery bacillus seems to be the causative factor even when no dysenteric infection can be demonstrated clinically. Though some cases are closely related to dysentery or enteritis, it is by no means the sole cause in the production of the syndrome. The disease deserves attention because of the essentially non-venereal nature of the clinical condition, and specially so, in our country, where great moral stigma is attached to persons suffering from venereal infection.

In view of the comparative rarity of the condition, the resistance to treatment, and the prolonged and self-limited nature of the clinical course, the following case is recorded:—

On 24th January, 1950, a man, aged 40, came for treatment with the chief complaint of having had a purulent discharge per urethra

which had started 3 days previously, accompanied by a slight smarting sensation during micturition. On trying to elicit a history of exposure to venereal diseases, the patient strongly denied any exposure and the denial was convincing. Smear examination of the urethral discharge was negative for gonococci. In spite of negative laboratory findings I started treating the case as one of gonococcal urethritis.

The patient was put on therapeutic doses of sulphathiazole tablets with the necessary precautions along with an alkaline and antispasmodic diuretic mixture. This was continued for about one week. Unlike what happens in cases of gonococcal urethritis, on the exhibition of sulpha group of drugs within the first few days, in the present case, even after a week's treatment, the degree of improvement was negligible. The smarting sensation had disappeared but the purulent discharge was persisting. Ten days after commencement of treatment, the patient developed fever and I was called in to see him. He was found to be running a temperature of 103°F.; the right knee joint was swollen, painful and tender, and the right leg could not be moved; he had also developed a bilateral purulent conjunctivitis which was characterized by absence of any pain or discomfort. The significance of these findings in association with his previous complaint of urethritis was at once realized and this led

to a revision of the diagnosis. As a result the patient was told about the non-venereal nature of his disease. In the light of the present findings an enquiry was made as to any previous history of acute dysentery but the patient did not remember to have ever suffered from any dysenteric disorder. He was put on intramuscular injection of 3 lac units of procaine penicillin G in aqueous solution (Crysticillin-Squibb) daily for four consecutive days, and for his conjunctivitis he was advised to use (1) normal saline to wash both eyes every 2 hours, (2) protargol drops twice daily and (3) unguentum HOF. to apply at bedtime. There was marked clinical improvement on the third day of penicillin therapy inasmuch as the patient was afebrile, his purulent urethral discharge had totally disappeared, his conjunctival inflammation was gradually clearing up but there was no apparent improvement in the condition of his inflamed and tender right knee joint. Expecting to hasten his clinical improvement, the patient was subsequently given two injections of N.A.B. 0.45 gm. intravenously on the 7th and 14th February but arsenical therapy failed to effect any appreciable improvement of his arthritis. His joint condition was his most incapacitating trouble now. He was given a course of non-specific protein shock therapy starting with bi-weekly injections of milk with iodine between the period of 20th February and 11th March. Medication during the whole period of treatment was on symptomatic lines and consisted of administration of salicylates, aspirin, etc., and local applications to the affected joint. When examined on 19th March, the patient was greatly improved and could walk about, but a very slight limp was still detectable in his gait. His treatment was discontinued and he was advised to carry on with his routine duties. When last examined on 17th April, he was found quite fit, active and normal without any residual deformity. The total period of disability from the onset of illness to complete recovery was about thirteen weeks.

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A CASE OF ACCIDENTAL PALUDRINE POISONING

By PARESH CHANDRA SEN, L.M.P.
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A GENTLEMAN working in the forest had an attack of fever. His associate advised him to take paludrine tablets two at a time three times a day. Unfortunately none of them was aware

that nowadays the manufacturers of the said drug are supplying 0.3 gm. in place of 0.1 gm. tablets. The gentleman had with him 0.3 gm. tablets, and as advised took two at a time, six tablets on the 1st day and felt nothing untoward on that day. Next day in the morning he took again 2 tablets, after that he felt some burning sensation and griping pain in his abdomen. In spite of it he took 2 more tablets in the noon and 2 in the night. As a consequence he had a very restless night, passing frequent tarry stools with intense burning and griping in his abdomen. The urine became scanty, high coloured and thick, there was burning of hands and feet and also slight perspiration over his forehead. He stopped taking further the paludrine tablets and went on taking plenty of plain water as well as liquid diet. The intensity of troubles lasted for three days even after the stoppage of the drug, and it took about a week to be free from all troubles.

The above history shows that paludrine, if taken in massive dose, can produce poisoning symptoms. The pathological state is located in the intestine only, producing irritation of the mucosa to such a degree as to cause hæmorrhage even. Simple withdrawal of the drug and plenty of water can cure the trouble.

In this connection I like to draw the attention of the manufacturers that in my practice I had been using 0.1 gm. tablets 4 times a day for several days, and do not remember to have come across any patient who complained of any intolerance to the drug. But since I have been prescribing the 0.3 gm. tablets, two tablets a day morning and evening, many of my patients are complaining of frequent loose motions together with griping pain, and as a result I had to stop it and prescribe some other antimalarial drugs for those patients.

I do not know why the manufacturers have withdrawn the former 0.1 gm. tablets. Those tablets had distinct advantages, and one could control the dosage according to the individual necessity and tolerance to the tablets. While in case of 0.3 gm. tablets one has to powder them and divide the powder which becomes unpalatable. I therefore hope that the I. C. I. Company will again introduce the 0.1 gm. tablets for the convenience of the patients.

[From the facts given in this case it is noted that the individual consumed 1.8 gm. of 'Paludrine' on the 1st day and 1.8 gm. on the 2nd day. The toxic side-effects described by your contributor fall into two main groups :

- (a) Gastro-intestinal effects.
- (b) Urinary effects.

These toxic signs agree closely with the results observed when the original research work was done on 'Paludrine'. N. Hamilton Fairley found (*Trans. Roy. Soc. Trop. Med. & Hyg.*, Vol. 40, No. 2, Oct. 1946, p. 143) that similar

effects to those described in this case were caused by dosage in excess of 1.0 gm. daily, but he remarked that these toxic effects were not serious and could be relieved by diminishing the daily dose of 'Paludrine', or cessation of therapy for two to three days.

Another report of a similar type appeared in your journal in the issue of August 1948 (Vol. LXXXIII, No. 8, p. 397) when Chakrabarti reported toxic effects (mainly gastro-intestinal) following a single dose of 1.2 gm. You then commented editorially that gastric irritation after a single heavy dose (1.2 gm.) was not surprising, and we think that your remarks on that occasion also apply to the case reported above.

With regard to the remarks about the 0.1 gm. tablets of 'Paludrine', we should explain that the 0.3 gm. tablet was introduced at the request and on the recommendation of the highest authorities, and this is the size of tablet best suited to the dosage now recommended by most authorities in this country. A full account of the reasons for introducing this new tablet was given in your issue of April 1949 (Vol. LXXXIV, No. 4, p. 180). If for any reason it is desired to give less than 0.3 gm., the tablet can be halved or quartered easily by breaking it. To facilitate this division of the tablet, we are shortly introducing a tablet having a double bisecting line which will facilitate division into halves or quarters.—J. M. Mungavin, M.B., B.Ch., D.T.M. & H. (Eng.), Medical Service Dept., I. C. I. (India) Ltd].

[We appreciate the device for divisions—
Editor, I. M. G.]

A CASE OF MYIASIS OF THE NASAL CAVITY

By SURJYA KUMAR BHOWMICK, L.M.F.

*Assistant Medical Officer, Telepara Tea Estate,
Binnaguri P. O., Dooars*

On the 30th March, 1950, a tea garden female labourer, aged 34 years, came to me with the complaints of epistaxis from the left nostril, swelling, pain, irritation and gnawing sensation in the nose. The trouble had started 3 days ago with slight pain and sanguineous running from the left nostril and on the day previous to her admission she had noticed a worm came out with the discharge. The patient gave a history of similar attack about 12 years ago. She had no fever on admission.

Irrigation of nasal cavities with turpentine in warm water was performed. Forty living worms were evacuated. The nose was plugged with a piece of cotton soaked in pure chloroform.

On 31st morning pain got worse and extended in the left-frontal region of the head. Swelling

and gnawing sensation increased and bleeding from the nose was continuous. No temperature. The nose was irrigated with strong solution of pot. permanganate in warm water. This brought out some 25 larvæ. The same treatment was carried out in the afternoon and 20 more worms were evacuated. This relieved her a little but she was not completely free from her pain. The temperature rose up to 100.2°F. in the afternoon. The nose was plugged with cotton-wool soaked in oil eucalyptus, and sulphonamide 2 tablets every 4 hours, 3 doses, were given by mouth. In the night the pain and gnawing sensation were so great that the patient could not sleep and passed a restless night.

On 1st April, morning temperature 98.6°F., redness and swelling increased over left lateral wall of the nasal cavity. I irrigated the nose with strong solution of pot. permanganate with chloroform water about double the strength of aqua chloroform B.P. This brought out more worms. In the afternoon the temperature rose up to 101.4°F. The pain became severe, redness, tenderness, swelling and gnawing sensation increased excessively over the nose and extended over the whole left side of the face indicating extension of inflammation through the frontal sinus and lacronasal canal. The same irrigation was continued, sulpha drug given by mouth and penicillin 200,000 units intramuscularly was given in addition. The following lotion was used for nasal drops and the nose was plugged with cottonwool soaked in it:—

Camphor 30 gr.
Chloroform 30 m.
Oil turpentine 30 m.
Oil eucalyptus 30 m.
Aqua distilled $\frac{1}{2}$ oz.

On 2nd April, temperature 100.2°F. in the morning and 99.4°F. in the evening. Redness, swelling, pain, tenderness and gnawing sensation became less. Six worms had come out of her nose in the night and 10 more worms were evacuated after irrigation. Sulphonamide 6 tablets during the day, penicillin 100,000 units morning and evening, and the same nasal plug and drops were put in.

On 3rd April, temperature remained normal and all complaints diminished markedly. The same treatment was continued and no more worms came out.

On 4th April, the patient did not have any rise of temperature and felt completely relieved of her trouble. The same irrigation and nasal drops were continued for about a week, and penicillin was stopped. The patient was cured completely.

My thanks are due to Dr. F. Mohler, Medical Officer, for permission to report this case.

Indian Medical Gazette

JULY

ABREAST WITH THE TIMES

IN the month of July 1950, after some 7 years, we are once again abreast with the times.

The reasons for having fallen behind the times were many. The lack of suitable material for publication, however, was not one of them. As a matter of fact, as things stand to-day, there is more material received every month than can be published in a single monthly issue, and we are considering the possibility of bringing out two issues in a month. More will be said on this possibility under 'Publishers' Notice' one of these days. After having come abreast with the times we intend going ahead of the times, at least so far as our sub-continent and our neighbours outside the sub-continent are concerned.

The advantage of a fortnightly issue are obvious. Some of our contributors have complained for years that for quick exchange of views they have to depend upon journals from outside India. Even for advertisement of newer drugs and instruments they have to depend upon these publications. 'Correspondence' and 'Any Questions' are definitely not news by the time the readers have seen the solutions of the problems in print (by letter we reply to them much earlier when such a reply is obviously indicated). For priority of an important observation, we put a date on the latter which is available in case of controversy. In fact this date is at times printed with the paper (received on . . .).

For the benefit of the readers who are holding drafts of articles, we reprint in this issue a request we made some time ago under the heading BETWEEN OURSELVES ON PREPARING A TYPESCRIPT, ETC. Such a concession in the draft will be specially helpful when the speed of the process from the manuscript to the formal printing is doubled.

Incidentally, the readers must have noticed that unlike most medical journals coming from outside the diction of articles in this journal is not uniform. It varies. In fact it varies from State to State, and so it should in fairness to the citizenship of the English words and expressions. If they are not going to leave our shores, they must live and move like other words and

expressions at the Centre and in the States, modifying and enriching themselves with shades and hues of at least four cultures: Dravidian, Vedic, Buddhist and Islamic. This will be their reward for the unification of the cultures themselves, and this will be our privilege in making the English language richer than we found it some 200 years ago.

We do not interfere with the genius of the writer apart from removing obvious errors of grammar and idiom and making the description consistent in itself. We have certain preferences but we do not impose them on the writer. For instance: (1) We prefer figures to words but the writers may choose either. They, however, should not use both in the same article. There is no harm in beginning a sentence with a figure and there is no rule of grammar against it. (2) We prefer cc. to cc.m. or ml. and no 's is necessary for the plural. The writers, however, may write what they like. It will be retained. (3) We prefer Gm. to gm. and recommend it; there will, then, never be any confusion between gm. and mg. Simple G. or g. should not be used.

Regarding the idiom, we advise the writer to discard it altogether. It is used at the best of times to hide an unpleasant or an incompletely known truth and has been used in the past in inventing cheap jokes against us. Even in the country of its origin it starts life as slang. Scientific people do not use slang.

Regarding the usage of 'a large number of experiments have shown', we hold with Fowler that the subject of the sentence is 'a large number' not experiments. Similarly 500 cc. of blood 'are bottled' not 'is bottled'. These usages are sanctioned by custom but we choose not to avail ourselves of the sanction.

Regarding the writer, he will find it more convenient to be 'the writer' or when a comparison is involved 'the present writer'. If he chooses to be 'I', we will allow him. A single writer, however, must not be 'we' unless he is taking the reader into confidence over some theory or plan. Whatever he begins by being he should remain throughout the communication, first person or third person.

Apart from such minor emendations we do not interfere with the account. Even the minor emendations may alter the intended meaning. In that emergency we consult the writer. Meaning should not be sacrificed to mere form.

We welcome criticisms of other writers, including ourselves, provided the tone is dignified.

We have recently got into touch with more writers than we did in the past. That is how we have truly come abreast with the times in another sense.

(Reprinted from *The Indian Medical Gazette*, Vol. LXXXIII, No. 6, June 1948, page 282)

BETWEEN OURSELVES ON PREPARING A TYPESCRIPT, ETC.

The paper economy has again become necessary. Your article, however, must be typed: (i) with a generous margin, (ii) in double space, and (iii) on one side of a sheet only. Not to do so is false economy as far as the ultimate expenditure of paper goes. Alterations made in editing on a sheet with narrow margin, typed in single space and/or on both sides of a sheet are not made out by the printer. They are undertaken again on the galley proof. Another galley proof may be required. Thus the paper is expended just the same with extra labour and irritation in dealing with the proof. The publication of the journal is also delayed.

As long as the need for the economy lasts, we will not insist on two copies of the typescript for our office, as long as you retain a copy which we may require. A typescript is hardly ever mislaid in our office. Occasionally, it is mislaid by the referee or in the press, or is lost in transit to and from them. Even these accidents are few and far between unless communal frenzy or labour excitement disturbs the routine of the town.

If for some reason or other single space typing is inescapable, the following conditions must be satisfied: (i) the margin should not be less than $\frac{1}{4}$ of the width of the page; (ii) after the final reading the typescript should be locked up in your drawer for two weeks to enable you to forget the syntax; (iii) it should then be read to you by someone other than your typist; (iv) all errors now detected should be corrected by pasting typed slips; and (v) typing on both sides of the sheet should be avoided.

If for some reason or other typing on both sides is inescapable at present, then kindly hold back your contribution as long as the economy lasts.

Under skiagrams and photographs should be pasted typewritten slips giving the legend. R and L, if wrongly placed on the former, should be stated to be so placed in the slip. Lately, several errors have occurred due to inversion and lateral inversion of the skiagrams.

The writing on figures and graphs should not be typed, such writing is not easy to photograph, in preparing the block.

We are mending our ways also. Due to economy in paper, we have not been acknowledging receipt of typescripts promptly and have been informing the contributors of the decision of the editorial committee only, later. This has caused annoyance and we express our regrets. From now onwards two intimations will be sent as formerly: one on receipt and one on deciding on publication.

Medical News

ELEVENTH INTERNATIONAL DENTAL CONGRESS FÉDÉRATION DENTAIRE INTERNATIONALE, LONDON, JULY 1952

THE Eleventh International Dental Congress of the *Fédération Dentaire Internationale* will take place in London in July 1952.

The Congress opens on Saturday, the 19th July, 1952, under the presidency of Dr. E. Wilfred Fish, and will include scientific papers, clinical and table demonstrations, scientific exhibits, films of dental interest, a dental trade exhibition and an oral hygiene exhibition. The Congress will close on Saturday, the 26th July.

The first day of the Congress will be devoted to the opening ceremony and receptions.

During the following week there will be discussions each morning introduced by the authors of papers which will have been published in the new *International Dental Journal* for this purpose.

The clinical sessions and table demonstrations will be held in the afternoons. Excursions, banquets and other social functions will be organized.

The *International Dental Journal* will be produced quarterly under the Editorship of Dr. H. H. Stokes, Professor of Dental Surgery in the University of Liverpool, and the papers to be introduced and discussed at the Congress will be published *in extenso* in the four issues preceding the Congress. The papers will be printed in English, but a list of contents, headings, legends to illustrations and summaries will also appear in French, German, Spanish and Italian. Its subscription price will be £2-5-0 per year, single copies 12s. 6d.; orders may be placed with Messrs. Cassell and Co., Ltd., 37/38, St. Andrew's Hill, London, E.C.4. The first issue will appear in September 1950. The Journal will include a Bulletin Section giving information about domestic affairs of the *Fédération Dentaire Internationale*.

Scientific Research Workers in any branch of Dental Surgery, Teachers and Dental Practitioners who wish to contribute to any of the sections of the Congress, should make enquiries from the Organizing Committee: Hon. Secretary, Mr. G. H. Leatherman, 13, Hill Street, London, W.1.

Every practising dentist possessing a legal qualification to practise dentistry in the country in which he received his professional instruction, or in the country in which he lives, may become an active member of the Congress on payment of the appropriate subscription. Medical Graduates and Licentiates and Members of other scientific professions may also be admitted as active members. Special arrangements will be made for Undergraduates in Dentistry and Medicine, Relatives of Active Members and Trade Exhibitors to become Associate Members.

Members of the F.D.I. may become members of the Congress and obtain the Journal at a reduced rate.

The American Express Co., Inc., will undertake the service of transportation of demonstration equipment, its storage, packing and custom clearance. Prospective visitors to the Congress can obtain information from the Office of the American Express Co., Inc., in their own country, which will also deal with hotel bookings and advise on any currency queries.

The Olympic Games in Finland take place the week after the Congress finishes in London, and visitors from distant parts will have the opportunity, if they so desire, of making the necessary arrangements to visit these games.

Further newsletters will be published at intervals.

The following four items are reproduced from Press Releases issued by the World Health Organization Regional Office for South-East Asia.

(1) THIRD WORLD HEALTH ASSEMBLY

FIRST WEEK OF MEETINGS

(No. SEA/PR/50-29, dated 19th May, 1950)

During its first week of meetings, the Third World Health Assembly, which is at present in session in Geneva under the chairmanship of Rajkumari Amrit Kaur, leader of the Indian Delegation, has already taken a series of decisions on policy, finance and programme of prime importance for the future of the World Health Organization.

In the first two days of general discussions delegates heard addresses by Mr. Trygve Lie, Secretary-General of the United Nations; Dr. Brock Chisholm, W.H.O. Director-General; Dr. Karl Evang (Norway), retiring Assembly President; the new President, Rajkumari Amrit Kaur and the leaders of a number of the 61 delegates present. On the third day the Assembly split up into two main working committees, the Committee on Programme and the Committee on Administration, Finance and Legal Matters.

COMMITTEE ON PROGRAMME

The Committee on Programme, which was under the chairmanship of Dr. Axel Hojer (Sweden), dealt with a number of important matters during the remainder of the week. The first of these was the four-year plan for world health which it is proposed to start in 1952. This plan, which provides for a thorough decentralization of W.H.O.'s work and is aimed primarily at strengthening and developing national health administrations, was accepted in principle by the Committee, which also requested the Executive Board to prepare a more detailed programme to be submitted to the Fourth World Health Assembly next year.

During the course of the debate on the four-year plan, a joint proposal was put forward by the delegations of India and Pakistan requesting that, in the plan, priorities should be established of the proposed activities, and emphasizing that special consideration should be given to graduate and under-graduate training of health personnel, to development of health and vital statistics and to the provision of medical supplies. Dr. J. D. MacCormack, of Ireland, warned against too ambitious a programme. Even Hercules, he said, confined himself in his infancy to tasks commensurate with his strength. W.H.O., an admitted 'infant prodigy', Dr. MacCormack added, should remember its youth in undertaking plans for future work. Dr. MacCormack also called upon the more advanced countries to make sacrifices now in order to provide vital assistance to less fortunately placed countries and supported the request from India and Pakistan for medical fellowships and training.

Another important subject discussed by the Programme Committee was the participation of the World Health Organization in the Technical Assistance Programme of the United Nations. It has been agreed that, as and when funds for the UN Programme of Technical Assistance are forthcoming, W.H.O. will share in them to the extent of 22 per cent, for health work in under-developed areas. It was decided to refer this question to a joint meeting of the Programme Committee with the Committee on Administration, Finance and Legal Matters.

The Programme Committee also considered the worldwide shortage of physicians and other health personnel, and the problem of attracting doctors from cities to rural areas. It recommended the Assembly to accept the views of the W.H.O. Expert Committee on Technical Education stressing preventive aspects of education of health personnel and suggesting standards of medical care and practice.

The Committee on Programme also reviewed the activities of W.H.O. in the fields of Fellowships, Exchange of Scientific Information, and Assistance to Educational Institutions.

COMMITTEE ON ADMINISTRATION, FINANCE AND LEGAL MATTERS

This Committee under the chairmanship of Dr. Johannes Holm (Denmark) took two important decisions during the remainder of the week. The first of these was to approve and confirm the cut in the 1950 budget for W.H.O. which had been made provisionally by the Executive Board last January. This means that, although the Second World Health Assembly authorized a budget of \$7,500,000 for the year 1950, actual expenditure will be kept below a ceiling of \$6,300,000. This decision was taken because of the fact that some contributions to the 1948 and 1949 budgets are still outstanding and also in view of the withdrawal of a number of Member States from the Organization which the Committee was told, constituted a serious budgetary handicap.

Mr. J. F. Hill, of Australia, called attention to the ceiling of \$1,900,000 which had been set by the United States Congress on the United States contribution to W.H.O. Although this question is now under discussion in the Congress, Mr. Hill pointed out, it would be unwise to anticipate a lifting of this ceiling. As matters stood, he added, the ceiling imposed on the U.N. contribution put it at \$600,000, less than the W.H.O. assessment for the U.S. contribution for the year 1950.

Turning to the financial report and accounts of W.H.O. for 1949, the Committee noted with satisfaction that the financial position of the Organization described by the W.H.O. External Auditor as being 'unsound' at the end of 1948, had improved somewhat during 1949. Uncollected contributions to the budgets of 1948 and 1949, which at the end of 1949 amounted to 17.85 per cent and 26.71 per cent of the total respectively, had been reduced by 30th April, 1950, to 15.45 per cent and 20.8 per cent, respectively.

The second important question dealt with was the application for membership of W.H.O. by Indonesia, Viet-Nam, Cambodia and Laos. The Committee decided to recommend to the World Health Assembly to accept these States as members. The matter will be dealt with at the next plenary meeting. In addition, the Committee decided to recommend the application from Southern Rhodesia for Associate Membership. As Southern Rhodesia is a territory not responsible for the conduct of its international relations, this application was sponsored by the United Kingdom.

Other matters dealt with by the Committee included that of the 18 countries which have not yet paid their contributions in full for 1948, and the 24 countries who are in arrears for 1949. It was decided to postpone action against these countries until the Fourth World Health Assembly, next year.

Finally, the Committee voted a resolution recommending to the Third World Health Assembly to elect a new Member State, entitled to designate a person to serve on the Executive Board for one year, to replace Byelorussia whose member has been absent from the Board meetings for the four last sessions. Seventeen members voted in favour of this resolution, fourteen voted against and there were four abstentions. In the preceding debate, delegates from Yugoslavia, India, Norway, Iran and Israel suggested that more time should be extended to the absentee members and favoured postponing action until the Fourth World Health Assembly, next year. The majority view was that the decision was not a discrimination against any member of W.H.O. but was necessary to preserve the integrity of the Organization. Delegates from the United States, Brazil, Canada, Belgium, and Australia, spoke in its support. Executive Board members from the U.S.S.R. and China have also been absent from recent meetings. Their term of office, however, expired with the present Assembly.

JOINT COMMITTEE ON PROGRAMME, AND ADMINISTRATION, FINANCE AND LEGAL MATTERS

This Committee held one meeting on Saturday afternoon. By a vote of 25 in favour, 2 against, and with 6 abstentions, it decided to propose a budget of \$7,300,000 to the Third World Health Assembly for 1951. A Canadian proposal to keep the level of expenditure for 1951 down to \$6,300,000 was defeated by 20 votes against and 9 in favour.

(2) W.H.O. MALARIA PROJECT IN AFGHANISTAN TO BE LAUNCHED BY INDIAN EXPERTS

(No. SEA/PR/50-30, dated 22nd May, 1950)

Two Indian scientists are leaving New Delhi to-day for Afghanistan under an engagement from the World Health Organization to launch a full-scale malaria-control project in the Khanabad-Khundus area in the north of that country. The two scientists are Dr. T. R. Rao of the Bombay State Malaria Organization, W.H.O. Team-leader, and Dr. S. L. Dhir of the Malaria Institute, Delhi, malariologist. Later in the year they will be joined by a W.H.O. Sanitary Engineer.

Dr. Rao last year led a small W.H.O. pilot malaria-control project in the Laghman district of Afghanistan. 'We shall have full co-operation and assistance from the Afghan Government', stated Dr. Rao on Saturday, 'and I am confident that within the next two years we shall succeed in controlling malaria among the 75,000 population in the 250 sq. miles area of the team's operations. This will enable the Afghan Government to go ahead with its plans for the economic development of the area'.

According to Dr. Rao, more than half the population of the area suffer from malaria each year. Although in this 'virgin territory' the species of mosquito responsible for carrying malaria has not yet been determined, it is known that the high incidence of the disease is to a large extent due to extensive irrigation.

Dr. Rao expects to begin DDT spraying operations by the middle of June. The team's transport, equipment, and a certain quantity of DDT have already been shipped into Afghanistan to await the arrival of the experts.

(3) INDONESIA JOINS THE S.-E. ASIA REGIONAL ORGANIZATION OF W.H.O.

WORLD HEALTH ASSEMBLY RESOLUTION ON CHINA

(No. SEA/PR/50-31, dated 31st May, 1950)

ON its own request, Indonesia is to belong permanently to the S.-E. Asia Region of W.H.O. which at present includes Afghanistan, Burma, Ceylon, The Republic of India, French and Portuguese India and Thailand. This was decided by the World Health Assembly when it admitted Indonesia and three other countries to membership at its Third Session which has just concluded at Geneva. Previously it had been understood that when Indonesia joined W.H.O. it would be part of the Western Pacific Region.

Viet-Nam, Cambodia and Laos, the other three newly-admitted members of W.H.O., will also form part of the S.-E. Asia Region subject to reconsideration when the Western Pacific Region is established probably before the end of 1950. All these countries will send delegates to the third meeting of the W.H.O. Regional Committee for South-East Asia to be held in Colombo, Ceylon, in September.

After discussion of a telegram announcing the withdrawal from W.H.O. of the Nationalist Government of China, the Assembly's Committee on Administration, Finance and Legal Matters passed a resolution stating that W.H.O. would welcome the resumption by China of full participation in the work of the Organization. Stressing the fact that W.H.O. is primarily interested

in people and not in the nature of their government, the authors of the resolution declared that what they had in mind was a wish for the full resumption of participation in the work of W.H.O. of the government which represented the Chinese people, whatever government this might be when China did resume participation.

The question of the withdrawal of the Nationalist Government of China from W.H.O. gave rise to an unprecedented discussion in the Committee which had before it another cable addressed to the Director-General of W.H.O. by the Peking Government of the People's Republic of China stating that Nationalist China had no qualifications for being represented on W.H.O. A proposal to reply inviting the Peking Government immediately to send a delegation to the current meeting of the Assembly was defeated by 16 votes to 2 with 12 abstentions.

Another recommendation of the Committee on Administration, Finance and Legal Matters was to reduce the assessment of the United States contribution to W.H.O. for 1951 from 36 per cent to 35 per cent of the total budget. The U.S. assessment for 1950 was last year brought down from 39.9 per cent to 36 per cent of the total. In principle, no member country should be required to contribute more than one-third of the total budget. An American Congressman, member of the U.S. delegation, said that this gesture on the part of W.H.O. would influence the U.S. Congress's attitude both towards the Technical Assistance Programme and towards the Bill now before Congress to raise the present \$1,900,000 ceiling set upon the American contribution to W.H.O.

A decision described by Dr. Brock Chisholm, W.H.O. Director-General, as 'the most important of any' was that the W.H.O. Executive Board will not be composed of Government representatives, but will continue, as laid down in the W.H.O. Constitution, to consist of technically qualified persons designated by Governments, and to act simply as the Executive Organ of the Health Assembly. Commenting on the Australian proposal to change the composition of the Executive Board, Dr. K. C. K. E. Raja (India) pointed to the 'profound and adverse effect' it would have on the work of the Organization, because national interests would naturally colour to some extent the decisions of the Board. Other delegates stated that Board Members should consider themselves as representing not their native countries but rather the entire world, and that the Board should continue, as in the past, to avoid political complications in its work.

With a view to lessening the drain on W.H.O. funds due to the heavy cost of meetings of the World Health Assembly, it was agreed in principle that Assemblies should be held once in every two years instead of each year as at present. A final decision on this question will be taken by the Fourth World Health Assembly next year.

Two decisions of special interest to Asian countries were taken by the Assembly's Committee on Programme. The first was the granting of top priority to the programmes for the control of pestilential diseases, especially cholera, plague and trachoma. The cholera-control programme of W.H.O. was transferred from the supplemental to the regular budget, while budget reductions in various other items were made in favour of disease-control programmes.

The second was taken following an Egyptian request that the Committee on Programme examine the need for emergency measures against the danger of cholera spreading into the Eastern Mediterranean Region through pilgrims to Mecca. Egypt asserted that the most recent cholera epidemic in Egypt (1947-48) was introduced from India.

The Committee decided that there was no emergency and that only 'a possible danger of a later emergency' would arise during the pilgrimage season (September 1950). Hence it was recommended that

an official approach be made by the Egyptian Government to the other governments concerned, namely India and Pakistan, stating the measures which, in the opinion of the Egyptian Government, it would be desirable for them to adopt before the commencement of the next pilgrimage season.

(4) FOUR NEW OFFICERS ARRIVE AT W.H.O. REGIONAL OFFICE

FIRST W.H.O. RECRUITS FROM ISRAEL AND THAILAND
(No. SEA/PR/50-32, dated 1st June, 1950)

Dr. H. G. MORIN, Malaria Expert, from the Health Services of the French Ministry of Overseas Territories, and Dr. Erb na Bangsang, for the last three years Director of the Division of Vital Statistics of the Department of Public Health, Thailand, both arrived in New Delhi to-day to join the permanent staff of the W.H.O. Regional Office for S.E. Asia. Other recent arrivals are Dr. L. R. Roberts, Tuberculosis Consultant of the British Ministry of Pensions, and Dr. Jacob Yofe, Malariaologist, from the Health Services of Haifa, Israel.

Last year Dr. Morin was attached as W.H.O. Malaria Consultant to the Far-East Headquarters of the United Nations International Children's Emergency Fund (UNICEF), Bangkok. In his new capacity of Malaria Adviser to the W.H.O. Regional Office in New Delhi, he will be in charge of the work of the six W.H.O.-UNICEF Malaria Control Teams now operating in India, Thailand and Afghanistan.

Dr. Roberts is to spend some time at the New Delhi Regional Office of W.H.O. before taking up his assignment as Tuberculosis Adviser to the W.H.O. Western Pacific Region.

Dr. Erb and Dr. Yofe are the first nationals of their respective countries to join the international staff of W.H.O. Their arrival brings up to ten the number of different nationalities represented at the New Delhi Regional Office. Dr. Erb is to assist Dr. R. L. Tuli (India), Regional Planning and Operations Officer, while Dr. Yofe will later take charge of a malaria control project in the Region.

RECORD PRODUCTION OF RADIO-ACTIVE ISOTOPES

BRITAIN MEETS WORLD DEMAND

BRITAIN'S Atomic Energy Research Establishment at Harwell is breaking all records in the production of radio-active isotopes. These are used in hospitals and laboratories throughout the world for medical diagnosis, treatment and research work.

There is such a demand from overseas that production is being still further increased. Exports of isotopes from this Establishment are already higher than that of any other atomic station in the world. At least 20 countries—ranging from the Far East to Western Europe—are being regularly supplied by air from Britain. During the month of March alone 473 packages of isotopes were sent abroad.

The British Ministry of Supply state that there has been an enormous increase in both the quantity and variety of radio-active materials being produced for industrial, medical and academic purposes. 'The total of consignments during the year was 3,443. About half the shipments consist of irradiated materials which do not have to be chemically processed. The other half are chemically separated in the laboratories. Some of the heaviest buyers of British-produced isotopes are Australia, South Africa, Sweden, Switzerland and Holland.'

SPECIAL CONTAINER

A special container which fits into the wing tip of aircraft has been designed for transporting atom

products by air. The container enables isotopes to be carried without the need for heavy lead shielding against radiation. So much weight is saved by this device that a single parcel can be reduced from 30 lb. to only a few ounces. This brings a corresponding decrease in transport costs.

The use of these isotopes made in Britain makes it possible for much medical treatment and research both in medicine and industry to be carried out which would otherwise be impracticable. They are sold by the Ministry of Supply at only nominal charges sufficient to cover the running expenses.

INDIAN COUNCIL OF MEDICAL RESEARCH

I.C.M.R. MICROFILM SERVICE UNITS AT THE CENTRAL RESEARCH INSTITUTE, KASauli, AND AT THE TATA MEMORIAL HOSPITAL, BOMBAY

EARLY in 1948, the Indian Research Fund Association (now Indian Council of Medical Research) set up a Microfilm Service Unit at the Central Research Institute, Kasauli, to supply microfilmed copies of articles from medical and scientific journals and periodicals required by various research institutions and research workers in this country. This Unit is capable of supplying microfilmed copies of articles from Indian and foreign journals which are available in any of the medical libraries in India. Institutions and organizations desirous of taking advantage of this microfilm service scheme were required to enrol as members of the scheme on payment of an annual subscription of Rs. 25. For this subscription, members were entitled to have any article which they require microfilmed at a charge of one anna per page plus postage.

The response so far to the microfilm service scheme has been very satisfactory. A good number of medical colleges, research institutes and other organizations have enrolled themselves as members of the microfilm service scheme. The Indian Research Fund Association have set up a second Microfilm Service Unit at the Tata Memorial Hospital, Bombay, to augment the existing microfilm service. The second unit will also be able to supply microfilmed copies of articles from any medical or scientific journal available in medical libraries in India.

In order to make available the services of these microfilm service units not only to scientific institutions and organizations but also to individual research workers, the Indian Council of Medical Research has decided to discontinue enrolment of members to the scheme on payment of annual subscription. The charges for microfilming work will now be made at a flat rate. The revised charges effective from the 1st April, 1950, are as under:—

Rs. 3 for the first ten pages or any portion thereof;	} plus packing and postage.
Re. 1-8 for every subsequent ten pages or portion thereof.	

It may be mentioned in this connection that in order to read microfilmed articles, an equipment called 'Reader' is required. Full information regarding the cost of this equipment and its supply can be had on request from Messrs. Kodak Limited, Kodak House, Hornby Road, Bombay.

All requests for microfilming work should be addressed to:—

The Officer-in-Charge,
I.C.M.R. Microfilm Service Unit,
Central Research Institute,
Kasauli,

or

Dr. V. R. Khanolkar,
Director of Laboratories and Research,
Tata Memorial Hospital,
Parel, Bombay 12.



BACK-ROOM-BOYS OF MEDICINE GET NEW HEADQUARTERS

After a wait of more than 10 years the 'back-room-boys' of medicine now have full facilities for their research into the common cold, influenza, radio-active isotopes, antibacterial chemotherapy and a hundred other subjects. They have just moved into their new ultra-modern National Institute for Medical Research at Mill Hill, London, officially opened by the King. Dr. G. M. Chu, Medical Officer from Shanghai, harvesting cold virus from infected eggs at the new headquarters.

UNESCO COUPON SCHEME

INFORMATION CIRCULAR No. 1

(UCS/Inf./1—page 2, 14th April, 1950)

BOOK COUPON SCHEME

Two more countries, Burma and Belgium, have recently joined the Book Coupon Scheme.

Burma has received a first allocation of \$15,000 worth of book coupons, which will be sold under the auspices of :

The Secretary,
Provisional National Commission,
Secretariat Buildings, *Rangoon* (Burma).

All booksellers in Burma are authorized to accept Unesco book coupons.

Belgium will participate as a vendor country only. All Belgian booksellers will accept Unesco book coupons.

This brings the number of countries co-operating in the Book Coupon Scheme to 13. These countries are as follows : Burma, Belgium, Czechoslovakia, Egypt, France, Hungary, India, Israel, Italy, Netherlands, Switzerland, United Kingdom (including British Colonial and Trust Territories) and U.S.A.

Italy.—We have now been informed that the distribution of coupons in Italy will be carried out by :

Italian National Commission for Unesco,
Villa Massimo, Largo di via Villa Massimo, 2
Roma (Italia).

FILM COUPON SCHEME

Belgium has joined the Film Coupon Scheme as a vendor country. Orders for films may be addressed to any supplier.

Egypt, already a member of the Book Coupon Scheme, has now announced its participation in the Film Coupon Scheme as a purchaser of films, and has received an allocation of \$10,000 worth of films. Film coupons will be distributed under the auspices of :

Administration of General Culture,
Ministry of Education, *Cairo* (Egypt).

There are now 5 countries taking part in the Film Coupon Scheme : Belgium, Egypt, India, Switzerland and U.S.A.

SCIENCE COUPON SCHEME

Egypt has also joined the Science Coupon Scheme and has received an allocation of \$20,000 worth of coupons for the purchase of scientific material. These coupons will be distributed by :

Administration of General Culture,
Ministry of Education, *Cairo* (Egypt).

This brings the participants in the Science Coupon Scheme to 4 : Egypt, India, Switzerland and U.S.A.

PRECISION INSTRUMENTS UNDER CONSTRUCTION IN DELHI LABORATORY RECORDINGS DURING HUNDRED THOUSANDTH PART OF A SECOND MAIN LINES OF SCIENTIFIC RESEARCH IN NATIONAL INSTITUTES

(From a Release dated New Delhi, 18th May, 1950, issued by Press Information Bureau, Government of India)

MODERN research, particularly in the domain of physics, calls for the construction and setting up of precision instruments as a preliminary to actual

investigation, and the National Physical Laboratory in New Delhi is at present engaged on this task.

Chief among these delicate instruments is the precision Beta Ray Spectrograph, now being built for studying the energy distribution of beta-radiations from radio-active substances. Many of the component parts, such as the power supply unit and linear amplifiers for simple and coincident counting, have already been assembled. These highly sensitive instruments are expected to record readings during infinitesimal by small periods, sometimes as small as a hundred thousandth part of a second. Besides being of fundamental importance, the results of this study may find important application in the field of medicine where many radio-active substances are used for diagnostic and curative purposes.

The construction of a quartz clock is also in hand. This clock, it is expected, will ultimately be controlled by an atomic clock providing a standard for the measurement of time which would be unaffected by known factors. For studies in optics, a number of optically plane and concave surfaces of substantial area, the largest about two feet in diameter, have been prepared. The reflecting surfaces are provided by extremely thin films of aluminium and other metals deposited by evaporation in vacuum.

Other investigations in the field of fundamental physics relate to the determination of nuclear magnetic moments by resonance of micro-waves and dispersion and absorption of ultrasonics in liquids.

In the sphere of applied physics, two important lines of investigation related to the preparation of carbon brushes and other carbon products; and, secondly, separation of some rare earths from one another and study of their luminescence when used as activators in suitable phosphor. These investigations are expected to find application in the preparation of luminous paints and gas mantles.

'SYNTHETIC RICE'

Some of the more important lines of research being undertaken in India's other National Laboratories are indicated below :—

The Central Food Technological Research Institute at Mysore is busy on a number of problems designed to improve the nutritional properties of subsidiary foodstuffs and to present the latter in forms acceptable to the ordinary man, for instance, production of 'synthetic rice' from tapioca, maize and jowar. The processing in this case is simple and permits of the use of food materials, some of which yield a better growth per acre than popular cereals like rice and wheat.

The National Chemical Laboratory at Poona is conducting experiments on the utilization of non-edible oils for technical purposes. These investigations are intended to modify tobacco seed oil and safflower oil for use in the manufacture of paints and varnishes, and some encouraging results have already been obtained. Castor oil on dehydration yields a material that is also of value in the production of paints and varnishes, but when subjected to prolonged heating, the oil is turned into an insoluble gel for which there is no known use. A method for obtaining a viscous liquid product from this gel has been explored, and experiments on the properties and uses of the viscous liquid are in progress.

Another line of investigation relates to the use of castor and other oils to replace coconut oil in soaps, without detriment to lathering properties. A promising composition has been evolved.

RARE METALS

In the Inorganic Division of the National Chemical Laboratory, new and quick methods of estimating rare

metals and minerals are being developed. Work has also begun with a view to concentrating precious metals and minerals from mixtures with less valuable materials. The chemistry of rare metals, particularly their analytical reactions, is being studied.

Processes for the manufacture of citric acid, calcium gluconate and vitamin C have been developed in the Biochemistry Division. The economic implications and technical aspects of these processes are now being investigated with a view to making the processes available to industry at an early date.

Experiments on animals have shown that a solution of a peculiarly pure gelatine is capable of overcoming shocks due to loss of blood without producing undesirable effects. Extension of this work, it is hoped, may provide possibilities of using this pure gelatine as a substitute for whole blood or blood plasma in surgical practice. Other investigations in this division relate to the preparation of Heparine, a drug derived from cattle liver. Attempts are also being made to produce carotene, precursor of vitamin A, by micro-biological digestion of leafy material.

COAL-WASHING

In the Fuel Research Institute at Dhanbad, investigations on froth flotation of Indian coals so as to reduce the ash content of high ash coals are being conducted, as also experiments for the reduction of their phosphorous content. Further tests are in progress on the subject of coal-washing, and a cyclone type of washer has been designed. Another line of investigation is the possibility of separating fractions of coals with reduced ash and improved coking characteristics from high ash coals by controlled breakage and subsequent screening. This is expected to result in separation of vitrinite from durain in coal.

Simultaneously, experiments are in progress to throw light on the polymeric constitution of coal. The coal sample is by suitable treatment converted into a number of fractions, which are subjected to chromatographic analysis for separation into homologous groups. The physical properties of these fractions are then determined. Constitution of tars is also being studied for obtaining fundamental data on coal bitumens.

'FOAM GLASS'

The Central Glass and Ceramics Research Institute in Calcutta has evolved a good thermal insulating material from waste glass. Styled 'foam glass', this is light and porous and its use in house construction should tend to reduce the effects of extreme heat and bitter cold. It is expected that the investigations will shortly reach a stage when commercial production can be begun.

The National Metallurgical Laboratory at Jamshedpur is evolving a process by which low-grade manganese ores can be converted into manganese sulphate for the production of high purity electrolytic manganese dioxide. Work on the control of grain size in austenite steels is being continued. This should lead to better use being made of imported metals, such as nickel and chromium.

The Building Research Unit at Roorkee has been concentrating on low-cost houses and conducting a series of investigations on sun-dried clay roofing tiles, soil cement floors and wall plasters from mud. A survey of clays used in the making of bricks in various parts of the country with a view to determining the compressive strength of the bricks is in progress. Lime sludge, a waste from sugar factories, is being tried as a stabilizer in the construction of walls and floors. How bamboo should be treated so as to serve as a substitute for steel in reinforcement of beams and concrete structures is another line of investigation.

The following 2 items are reproduced from Releases issued by British Information Services, Office of the U.K. High Commissioner in India.

(1) NEW USES FOR PLASTICS

WIDE APPLICATION IN MEDICINE

By TREVOR I. WILLIAMS,

Deputy Editor of the Scientific Journal 'Endeavour'
(No. B.F. 576)

THE importance of plastics in the modern world is even greater than their common uses indicate. The ordinary domestic uses in electrical appliances of every kind, cups and saucers and other kitchenware, containers and wrappings for all sorts of everyday goods and the almost innumerable other applications with which everyone is familiar reveal only a part of the story of plastics.

Apart from these, plastics find many applications which the general public rarely realizes. All kinds of technical equipment—for example, those used in television, x-ray work, chemical research and engineering—are to-day made partly or wholly from the many different varieties of plastics available. Plastics is not a precise term; it involves a whole range of widely differing substances just as the word 'wood' denotes all kinds of varieties as different as balsa, ebony, oak and pine.

Medicine in particular has been quick to take advantage of the exceptional properties of plastics. All sorts of orthopaedic equipment, splints, replacements for bone bandages and sutures for closing wounds have been made from plastic materials. Very recently still another and quite different medical application has been developed—that of taking casts of insides of anatomical specimens which are not otherwise easily reproducible and of making quickly and simply exact reproductions of other complete structures such as bones.

IMPORTANT DEVELOPMENT

This important medical development, to which the Institute of Orthopaedics of London University has made valuable contributions, depends primarily upon the use of a relatively new type of plastic, called polyester resins, which have previously found quite different uses, for example, in making electrical insulators, the hulls of boats and components for aircraft.

Chemically, these plastics are very complex. The reason for their particular importance, however, is quite easily stated. It lies in the fact that—unlike most plastics which have to be cured by considerable heat—they will set in the cold to a pale yellow transparent solid. All that is necessary is to mix two liquids together giving a syrupy solution which will keep for 24 hours or more and then stir in a third liquid called 'accelerator'. The accelerator causes the liquid to set solid in about an hour without any further treatment.

A typical example of the use of this type of plastic is in exploring the complex system of blood vessels inside an organ such as the lung of a sheep. The liquid resin is drawn in slowly until the veins and the arteries in the lung are full; then it is left for a few hours to solidify. Then the tissue is dissolved away with acid and a detailed solid replica is left of the blood vessels and the air spaces within the lung. By first colouring the plastic drawn into each part of the specimen with suitable pigments it is possible to distinguish clearly the different parts of the structure by different colours.

TWO ADVANTAGES

This interesting technique has two important advantages. In the first place, it makes it possible to make for teaching purposes exact models of normal structures which are not otherwise easily described or dissected. Secondly, it enables a permanent record to be made of the abnormalities of a structure which are rarely encountered but which it is important to understand for future diagnoses.

Interesting and important though it is, this modelling of complex internal structures by no means exhausts the medical possibilities of this type of plastic. It can be used, for example, for making replicas of small objects such as bones. For this purpose a different type of plastic is needed in addition. This is one that melts at a low temperature and then sets on cooling to a very flexible rubbery solid.

The object to be modelled is suspended in a liquid form of plastic and then set aside to cool. When the plastic material has set solid, the object is easily removed, leaving a cavity which exactly follows all its contours. This cavity is then filled with liquid polyester resin and the mould is set aside until the liquid has solidified. Then the solid plastic is removed from the flexible plastic mould and emerges as an exact duplicate of the original bone or other object. If desired, an appropriately coloured pigment can be included in the liquid polyester resin so that the models are of the same colour as the originals.

OTHER USES

Another important medical use of these versatile polyester resins is in the mounting of anatomical specimens. Specimens of all kinds can be embedded in liquid resin and when this has set solid the object, firmly embedded in the glassy solid, can be freely handled and examined without the slightest risk of damaging it.

Still another use of this type of plastic is in making surgical splints of all types, especially those which are of unusual shape. Layers of cloth, preferably cloth woven from glass fibres, are soaked in liquid resin and are then allowed to set solid, leaving a perfectly rigid splint of the desired shape.

To say that we live in a plastics age is an exaggeration, for conventional constructional materials such as metals and wood continue to play a dominant rôle in daily life. Nevertheless, it is certainly true that, perhaps to an even greater extent than is usually recognized, plastics have a powerful and steadily increasing part to play in almost every aspect of our lives.

(2) SIR EDWARD MELLANBY,

Director of India's National Drug Institute
(No. B.F. 580)

SIXTY-SIX-YEAR-OLD Sir Edward Mellanby, who has been appointed Director of the Central Drugs Institute, Lucknow, is one of Britain's foremost medical scientists. Three years ago he was awarded the Buchanan Medal of the Royal Society 'for his services to medical science and in recognition of his outstanding researches on dietary factors'.

He has been a pioneer in the study of diet and nutrition and for the last 16 years he has carried on his work concurrently with directing medical research throughout Britain, for he is Secretary of the Medical Research Council.

Born at West Hartlepool, County Durham, in 1884, he was educated at Barnard Castle School and Emmanuel College, Cambridge, where he was a scholar, research student from 1905 to 1907, and later on an honorary fellow. He took his M.A. and M.D., doing

his hospital course at St. Thomas', London, where he afterwards began his teaching career as Demonstrator in Physiology. From 1913 to 1920 he was Lecturer and later Professor of Physiology in London University (King's College for Women); he then went to Sheffield as Professor of Pharmacology until 1933, when he received his appointment as Secretary to the National Medical Research Council. He had been a member of the Council for two years. In 1935 he was elected Fullerian Professor of Physiology to the Royal Institution.

RESEARCH ON RICKETS

One of Dr. Mellanby's early pieces of research concerned the physiological effects of alcohol, an investigation which he undertook for the Government during the first World War. Around this time the late Sir Frederick Gowland Hopkins was carrying on his research which led to the determination of the vitamins, and Dr. Mellanby also did pioneer work in this field. By dietetic experiments on puppies he found that rickets was caused by an absence from their diet of a fat-soluble substance which controlled the deposition of calcium in the bones. This anti-rachitic substance later received the name of vitamin D.

In 1925 the Medical Research Council published a report of further experiments by Dr. Mellanby on these lines, establishing the fact that bread and cereals tended in themselves to cause rickets; later he identified the rachitic substance in a cereal diet as phytic acid, and found that it could be counteracted by adding vitamin D or extra calcium. A later series of publications demonstrated that actual bone changes in shape could be caused by faulty diet; following up this line Sir Edward—he received the K.C.B. in 1937—proved that lack of vitamin A causes abnormal bone growth and neurological disorders due to pressure of the overgrown bone. His investigations have included a study of the effects of lack of iodine; and one of his researches demonstrated that bread made from flour bleached chemically by the Agene process (NCl₃) can cause the condition in dogs known as canine hysteria.

In 1925, Dr. Mellanby was elected a Fellow of the Royal Society. He had become a recognized authority on nutrition, and was member of successive committees appointed to advise the Ministry of Health. He worked for the League of Nations, was Chairman of two International Conferences for the Standardization of Vitamins and of the International Technical Commission on Nutrition.

Sir Edward Mellanby was Honorary Physician to the King from 1937 to 1941. He held many other important positions during World War II. He was chairman of a committee which investigated and advised on the health of Flying and Naval personnel and has been since 1940 a member of the Scientific Advisory Committee to the Cabinet. In 1941 he was appointed a member of the Colonial Products Research Council, and in 1945, chairman of a medical research committee to advise on colonial problems.

LADY MELLANBY'S WORK

Sir Edward Mellanby's wife, whom as May Tweedy he married in 1914, is like himself a distinguished scientist.

Lady Mellanby has specialized in research on the effect of diet on dental health; the Medical Research Council published a three-volume report by her on this subject between 1931 and 1934. Her work on the teeth of London school children has been outstanding.

She is an honorary member of the British Dental Association, and an investigator for the Medical Research Council; in 1935 she and her husband were jointly

awarded the Charles Mickle Fellowship of the University of Toronto.

CLIFFORD DOBELL, M.A., Sc.D., F.R.S.

(Reproduced from *British Medical Journal*, Saturday, 14th January, 1950, p. 129)

THE death of Clifford Dobell in London on 23rd December, 1949, has deprived the scientific world of an outstanding protozoologist, who in his brilliant studies of the intestinal amœbæ of man made important and lasting contributions to tropical medicine.

Born in 1886, he was educated at Sandringham School, Southport, and at Trinity College, Cambridge. He graduated B.A. with first-class honours in the natural sciences tripos in 1906. In 1910 he proceeded to the M.A. and ultimately, in 1912, the Sc.D. While at Cambridge, Dobell studied zoology under Adam Sedgwick, continuing his training abroad—under Richard Hertwig at the Munich Zoological Institute, at the Zoological Station in Naples, and in Ceylon. In 1908 he was elected a Fellow of Trinity College. He was awarded the Walsingham Medal of the University, and he was a Rolleston Prize-man, Oxford and Cambridge, and a Balfour student of Cambridge. Even as an undergraduate, Dobell had begun to specialize in protozoology, and he wrote his first papers on the parasitic protozoa of lower animals in 1907; other publications followed devoted to protozoa, bacteria, and spirochaetes in 1910; he was appointed assistant professor of protistology and cytology at the Imperial College of Science, London, a post which he held until 1919. There he continued his researches on the protozoa of lower animals, but the 1914-18 war turned his main interest to the human intestinal protozoa, and especially the amœbæ. On this subject he soon became one of the foremost authorities in the world. When, in 1915, the War Office started a scheme for training protozoologists in the diagnosis of amœbiasis, Dobell was appointed to take charge of the classes which were held at the Wellcome Bureau of Scientific Research. From this period he devoted himself uninterruptedly to investigations of the intestinal protozoa of man. He was one of the first to demonstrate the existence and to appreciate the epidemiological significance of symptomless carriers of *Entamoeba histolytica*, whose number among the inhabitants of Great Britain he estimated at 10 per cent. He standardized the methods of parasitological diagnosis of amœbiasis, revised the morphology and classification of the human amœbæ, and played an important part in bringing about improvements in the treatment of amœbiasis with emetine. Such was the excellence of the work that in 1918—at the early age of 32—he was elected a Fellow of the Royal Society.

In 1919 he published his classic monograph, 'The Amœbæ Living in Man'. This book, though written thirty years ago, is still an indispensable source of accurate information for all serious workers in tropical medicine. Dobell became protistologist to the Medical Research Council at the National Institute for Medical Research in the same year, and there he remained till his death. His next work of medical importance was 'The Intestinal Protozoa of Man', published in 1921. Originally conceived as a joint work with and bearing the name of F. W. O'Connor, it was actually written entirely by Dobell. The book provided a valuable practical guide to all the intestinal protozoal infections. At that time the complete life histories of the human amœbæ were still unknown. The discovery by Boeck and Drbohlav in 1925 of suitable culture media enabled Dobell to carry out a series of remarkable investigations, published under the general title 'Researches on the Intestinal Protozoa of Monkeys and Man'. In

these papers which appeared between 1928 and 1943, Dobell not only described the full life-cycle of all but one (*Iodamoeba*) of the human amoebæ, but also established their identity and interchangeability with those of macaque monkeys. Apart from these contributions to medical knowledge, Dobell wrote numerous papers of zoological interest, and made many contributions to the history of protozoology, including his masterpiece *Antony van Leeuwenhoek and his Little Animals*.

Clifford Dobell carried out all his investigations with painstaking thoroughness, while his published works were always perfect in literary style and bore the mark of wide erudition and scholarship. By nature he was retiring, shunning the limelight, and content to devote all his time to scientific and literary pursuits in the seclusion of the laboratory and the study. But he was always ready to share his encyclopædic knowledge with those who sought his advice. He was respected universally and admired by many, though a few were resentful of his outspoken criticisms. Many of us will remember him as a loyal and generous friend.

Dobell belonged to many scientific and medical societies at home and abroad, and served at various times on a number of committees. He married in 1937 Monica Baker, who was the step-daughter of his old friend, the late Dr. William Bulloch, F.R.S.—C. A. H.

COLONEL H. E. SHORTT, C.I.E., I.M.S. (RETD.)

(Reproduced from *The Medical Officer*, No. 2174, 25th March, 1950, p. 113)

COLONEL H. E. SHORTT, C.I.E., I.M.S. (Retd.), Professor of Medical Protozoology in the London School of Hygiene and Tropical Medicine (London University), has been elected a Fellow of the Royal Society.

CANCER HOSPITAL IN CALCUTTA

(Abstracted from the *Journal of the Indian Medical Association*, Vol. 19, No. 6, March 1950, p. 235)

INDIA had many problems to solve for the prevention and cure of disease, and it was of fundamental importance for her not to depend on foreign industries for the production of substances such as vaccines and antibiotics, said Mme Joliot-Curie, opening the Chittaranjan Cancer Hospital in Calcutta on 12th January, 1950. She also laid the foundation stone of the nurses' home of Chittaranjan Seva Sadan.

Mme Joliot-Curie went round wards and departments of the Cancer Hospital and showed particular interest in the million volt x-ray unit there.

She said that, since the first use of radium for the therapeutics of cancer which was made in France a few years after the discovery of radium, many big centres had grown for the treatment of the disease by radiation. It was a great pleasure for her to see the birth of a big medical institution for cancer treatment in India.

Cancer was not a tropical disease, but occurred frequently everywhere. It seemed to her that India had many superficial cancers which were among those that could be cured relatively well by the use of radium or x-ray. The work of the Cancer Hospital should therefore be particularly fruitful.

Big medical institutions were useful not only for routine medical work, they must also be centres of medical research. A centre for the preparation of vaccines could improve the efficacy of known vaccines or make new ones, and that for the manufacture of penicillin or streptomycin could study the action of these antibiotics on different diseases or perhaps find new antibiotics.

In a centre for the treatment of cancer, even simple statistics of the origin of cases and their treatment could be the basis of important medical progress. Dr. Khanolkar of Bombay had shown that many cases of cancers of skin or tongue were due to permanent irritations resulting from particular ways of living and could be easily avoided.

Comparison of the statistics of the nature of cancers in a tropical country, whose conditions of life were different from those in Europe and America, could help to throw light on the origin of cancer and perhaps lead to means of prevention of the disease.

Mme Joliot-Curie hoped the Cancer Hospital would devote some of its activities to the research essential for the progress of therapeutics and of pure science.

Dr. Roy, West Bengal Premier, who presided over the occasion, recalled how out of charities Chittaranjan Seva Sadan and now the Cancer Hospital had grown up. It was in the fitness of things that Mme Joliot-Curie, who by her researches had established the reputation of being one of the foremost scientists of the world, should open the hospital.

PRESS INFORMATION BUREAU, MINISTRY OF INFORMATION AND BROADCASTING, GOVERNMENT OF INDIA, CALCUTTA

Press Note

QUARANTINE RESTRICTIONS

INFORMATION has been received by the Director-General of Health Services that the health authorities in Jordan have declared Delhi as infected with cholera.

In order to avoid delay and inconvenience on entry into Jordan, passengers leaving Delhi by air and surface transport for Jordan are advised to be in possession of cholera inoculation certificates showing that inoculation has been performed not less than seven days and not more than six months prior to arrival in Jordan. The inoculation should be given in two doses with an interval of seven to ten days between the two doses. The certificate should be in the international form, signed or countersigned by a medical officer in Government or municipal service.

Director-General of Health
Services,

New Delhi, 12th July, 1950.

HCB/Cal. 35, 12-7-50.

Press Note

QUARANTINE NOTICE

Information has been received by the Director-General of Health Services that the health authorities in Malaya and Singapore have declared Calcutta as infected with plague. It is, however, not necessary for passengers to provide themselves with plague inoculation certificates.

Director-General of Health
Services,

New Delhi, 12th July, 1950.

HCB/Cal. 35, 12-7-50.

Public Health Section

MATERNITY AND CHILD WELFARE WORK IN RAILWAY COLONIES

By B. L. CHOPRA, D.P.H., D.T.M. (Liverpool)
Dist. Medical Officer, E. I. R., Kanchrapara

THE subject is divided below under different heads and sub-heads with a view to simplification and in the hope that the simplification will help in organizing maternity and child welfare work in railway areas. This subject is gaining great importance since India has attained her freedom. Recently a symposium on maternal and child health work in India was opened for four days on 30th December, 1949, under the patronage of Hon'ble Rajkumari Amrit Kaur.

A. ACCOMMODATION, STAFF AND ORGANIZATION OF A CENTRE

A useful Maternity and Child Welfare Centre should normally consist of two good rooms, one for the lady doctor and the other for the lady health visitor. There should be a grass lawn, small flower garden with a compound wall. On the grass lawn a few outdoor children sports like see-saw should be installed. The staff should consist of a lady doctor, a lady health visitor, an ayah, a female sweeper and a peon. As regards equipment it is essential to have a maternity examination table, baby weighing machine, arrangement for washing and bathing of the infants, instruments like pelvimeter, forceps, douching can, etc., and a few useful medicines for infants. Facilities for douching should also exist. The rooms should be decorated with useful posters and pictures on the subject. By experience it is found that it is no use leaving the centre in charge of midwives who are really not up to the mark. On the N.W.R. it was customary to have a lady doctor and lady health visitors in charge of the Maternity and Child Welfare Centres at the Divisional Headquarters. In case of other small hospitals and dispensaries these centres were left in charge of midwives but by experience it was found that such centres did very little useful work. Properly trained lady health visitors were considered necessary if these centres were to be made useful and popular. Then there has been some controversy about having lady doctor or lady health visitors in charge of these centres. It was found by experience that both these ladies are essential for running of such a centre. Lady doctors take up the curative side of the work whilst lady health visitors the propaganda and educative side of the work as well as training of the midwives. Each centre should be provided with printed cards for keeping a record of the mothers, infants, toddlers and children visiting the centre. The staff should be controlled by a Maternity

and Child Welfare Council which may be formed in every railway colony. Besides controlling the staff of these centres these councils can do educative work by enlightenment of the mothers on the subject and dispel superstitions. By experience I find that these councils should be formed from amongst the ladies of the colony with the head medical man in the colony as the Honorary Secretary of the Council. The seniormost lady becomes the president and the others elected as vice-presidents and members by annual voting from amongst the registered members of each centre. The vacancy caused by any member of the council leaving the centre on transfer or otherwise should be filled by the council by voting. Besides these executive councils, a Central Maternity Council for each railway with the chief medical officer as its chairman should also be formed with an accounts officer and a personnel officer as members. The local Maternity Council should meet once a month and Central Council once in three months. Each local council should send their delegates to Central Council at their quarterly meetings. Members of the local councils should in turn be the visiting members of the centre for one month. They should supervise daily the bathing and washing of babies, distribution of milk to the needy children, treatment of ailments by the staff of the centre. The Central Maternity Councils should frame general rules for running of these centres on each railway and local councils have their by-rules wherever necessary to suit local conditions. To stimulate further interest in these centres, annually Baby Health weeks should be organized and prizes given to best babies. Educative films on these subjects should also be exhibited during these health weeks. Charity dances and shows should also be organized to collect funds for providing useful addition for the centre. I organized such charity dances at Lonavla (Poona district) beginning with the year 1927 and also at Ferozepore beginning with the year 1942. In one year at Ferozepore we collected some five hundred rupees and amongst other useful things purchased from this money was a cow for the centre to provide pure milk to needy and poor children.

B. WORK DONE IN THE CENTRE

The work in these centres is usually divided into ante-natal work, post-natal work and house visits. I will describe below in brief maternity and child welfare work in railway colonies under these three headings :—

I. Ante-natal work

This mainly consists of advice on the nutrition for the mother and the 'expectant newborn'.

Emphasis concerning nutrition in pregnancy has always been on its maternal aspects. But in the light of recent developments advice on nutrition for the 'expectant newborn' should be equally stressed.

Diet of the expectant mother

Needs of expectant mothers: From the start of pregnancy expectant mothers need increasing amount of proper nourishment. During this period the exact daily requirements of proteins, carbohydrates, fats, vitamins and minerals should be based on the following three principles:—

(i) To correct existing maternal nutrient deficiency as quickly as possible.

(ii) To compensate for the physiological changes in pregnancy as they affect the expectant mother and possibly to abort some complications of pregnancy.

(iii) To supply the nutrients for the proper formation, development and growth of the expectant newborn.

Generally speaking the following deficiencies are most important: (a) night blindness and xeroses due to deficiency of vitamin A, (b) disturbances in sensation of the feet, legs and hands with muscular weakness (thiamine), (c) inflammation of tongue and skin troubles (nicotinamide), (d) disease of the gums due to deficiency of vitamin C, (e) disease of the eyes, ears and oedema with flattening of the tongue papillæ due to deficiency of riboflavin.

The level of vitamin C in the maternal blood falls progressively as pregnancy advances because of the demands of the foetus. Vitamin C deficiency as above stated harms the teeth and gums and causes gingivitis in the expectant mother. Vitamin D is needed to prevent maternal osteomalacia.

It cannot be definitely stated whether poor nutrition is the cause of emesis or hyperemesis gravidarum though there are reports which link the two and thiamine has been given with advantage in these conditions. Then there is evidence to show that nausea of pregnancy is benefited with the use of pyridoxine hydrochloride though no actual deficiency of this vitamin has been shown early in pregnancy. In my experience Esdavite capsule (Sharp and Dohme), one daily, is very useful for expectant mother and expectant newborn as it contains all the abovementioned vitamins. Contents of each Esdavite capsule are given in the following table which also gives the minimal daily requirements.

Mineral requirements for the expectant mother

(i) *Calcium*.—There is retention of about 45 gm. of calcium during pregnancy of which one-half forms a reserve in the bones of the expectant mother for lactation. The necessary

	Esdavite capsule	Daily requirements
Vitamin A ..	20,000 units	4,000 units
Vitamin D ..	2,000 units	400 units
Thiamine hydrochloride.	5 mg.	1 mg.
Riboflavin ..	10 mg.	2 mg.
Pyridoxine hydrochloride.	1 mg.	No standard yet fixed.
Calcium pantothenate.	10 mg.	Do.
Niacinamide ..	50 mg.	Do.
Ascorbic acid ..	150 mg.	30 mg.
Mixed tocopherols	10 mg.	No standard yet fixed.

needs for calcium are better obtained and utilized from natural foods. Calsid is recommended for ante- and post-natal calcium deficiency.

(ii) *Iron*.—In true pregnancy anaemia diet plays an important part in prevention and correction. The pregnant mother generally absorbs 2 to 10 times more iron. Whatever the cause, every effort should be made to correct existing anaemia in early pregnancy. Later 18 to 20 mg. iron intake per day is required and can usually be secured from regular foodstuff. Polyhaemin tablets in my experience are excellent for this purpose if any drug is required.

(iii) Use of folic acid and crude oral liver extract and an increase in proteins are also helpful.

(iv) *Iodine*.—Iodine is useful during pregnancy due to increase in metabolism, particularly in areas where goitre is prevalent.

For successful lactation expectant mother should store essential proteins, vitamins and minerals during ante-natal period by ample daily intake.

Diet suitable to help the expectant newborn

Coming to the nutritional needs of 'expectant newborn' (the term used by W. F. Guerriero in *Texas State Journal of Medicine*, May 1949), it should be noted that

(i) There is progressive increase of the needs of vitamin A in the expectant newborn liver as pregnancy advances.

(ii) Riboflavin is also essential for normal growth of the foetus. Abnormal children are sometimes born due to nutritional deficiency in the mother as this arrests the developments of the expectant newborn.

(iii) The foetus draws on the mother for its requirements of vitamin C. The effect of vitamin D in the maternal diet requires further investigation. It helps the utilization of calcium. Vitamin D in human milk is also an important factor in preventing rickets more than the minerals. Vitamin K has been administered to the pregnant mother shortly before and

during labour to influence the concentration in the blood of the newborn but this has recently been given up.

(iv) Amongst the *mineral requirements* calcium and phosphorus require to be increased with the life of the expectant newborn and during the period of its growth.

Congenital rickets and imperfect bony structures in the infant have been noted in association with calcium, phosphorus and vitamin D lack in the diet of the expectant mother. The structure of the deciduous teeth is also affected by the content of calcium, phosphorus, vitamin D and proteins in her diet. She generally begins pregnancy in a negative calcium balance and should immediately be given good quantities of calcium, phosphorus, vitamin D and protein in the formation period.

Radio-active iron appears in the expectant newborn circulation within forty minutes after administration to the mother.

(v) Protein requirements of the expectant newborn require consideration. The foetus requires large amount of proteins. Progressive increase in the birth-weight and length with increasing amount of proteins in the diet is quite striking. Then there is also strong relation between protein availability for the expectant newborn and prematurity, immaturity, stillbirth, abortions, deciduous teeth and imperfect osseous structure development. The foetus is parasitic for its protein needs only to a certain degree. As soon as the protein stores of the mother are exhausted to any major degree, she retains the remaining stores due to some protective mechanism. Thus an adequate daily intake of proteins from the natural foods by the pregnant mother, particularly in the growth period when there is greatest demand of proteins for herself and the expectant newborn, is essential.

II. Post-natal work

(a) How to lower infant mortality

During the first year of existence infant mortality reaches a very high level. Attempts have been made to put it down to nature. It is, however, an error to consider mortality as natural expediency since it is noticed that not only those who are born weaklings but those who are born healthy perish if proper food and care are not administered to them. The contrary is known to be the fact. With proper nourishment and treatment those who are born before their time or born weak may be made to survive. Amongst the railway staff ignorance and obsolete tradition are great factors which cloud the sense of infant feeding and care, which are handed down to the young mother by every grandmother. Therefore it is necessary that the object of post-natal welfare should be achieved through publicity and guidance given to the mother so that the infant's normal growth may be bettered. Hence is the necessity of extensive

enlightenment of the mother on the subject. This work should be entrusted to Maternity Welfare Council which may be started in every railway colony to dispel the superstitions.

(b) Welfare of the child after birth

Such councils will achieve their purpose most if instructions regarding the proper feeding and care of the infants are given to the mother and she is also instructed to have periodical medical consultations. It, therefore, becomes very necessary that in organizing these centres we should, in addition to a lady health visitor, have a lady doctor as stated in the first para before attached to every Child Welfare Centre. The growth of the child can be watched if it is regularly examined at the centre and entered on post-natal cards. It is necessary that a young and inexperienced mother should be able to recognize from the start the illness or disorders of the child. The young mothers often get very panicky about every ordinary ailments of the children. The medical person attached to the centre should be able to give advice on prognosis and the prevention of the child's disease.

Then again it is very necessary that proper understanding or precautionary measures for the newly born are to begin early as infant mortality is known to be at its highest during the first month of its existence. The mother should be advised as to what constitutes a proper food and as to how she should conduct her life just before delivery.

(c) Welfare of the mother and child at and after delivery

The mother should always be instructed to nurse her newly born baby. The mother's milk is the best and the most suitable form of nourishment for the suckling. The greatest number of infants are known to die in the first month owing to incidental chills. In my experience it is chiefly those children who are fed on artificial food that fall victims to the disease of digestive system but those who are breast-fed rarely suffer from such complaint.

Some advice on weaning is also necessary. As a rule this is an easy matter for the majority of the mothers. Only slight inconvenience felt on the first day.

(d) Hints regarding baby's feeding and dwelling

During the summer infant mortality reaches a high figure. Not only in a hot climate but in overheated places the baby who is warmly clad, runs the danger of being too warm. The regulation of children's body warmth is also endangered when they suffer from stomach trouble and are exposed to overheating at the same time.

The question of baby's dwelling is also of very great importance and it is commonly known

that much is left in this direction by parents to be decided by lady health visitor who should advise the parent rightly because unhealthy conditions present still another danger. The adults who are suffering from cold, cough or from other chest troubles and who share the same living space with infants may infect the latter. In case of chest trouble it is advisable to keep apart infant from the grown-up especially if the latter is also entrusted with feeding or looking after it. Infection may be prevented with the help of layers of gauze and may be advocated by lady health visitor in suitable cases. The lady health visitor should use her discretion in such cases according to the circumstances of each case. She should explain to those concerned that the babies are helpless in this matter as they are not equipped with the power of resistance and that they should be protected against the danger of their surroundings. Their nourishment and fostering should be done in the best possible way.

The infant during the suckling period has difficulty in maintaining its iron balance. For the first six months of life the infant is dependent on its iron stores secured during its life as an expectant newborn. Failure of the foetus to store iron may result from anaemia in the expectant mother.

(e) *British method of supplying vitamin requirements of mother and child after its birth*

About two years ago I saw a circular from the British Ministry of Food. The Ministry of Food in conjunction with the Ministry of Health and Secretary of State for Scotland announced that from 1st August, 1947, every mother will be entitled under the Welfare Food Services to vitamins A and D tablets free of charge for thirty weeks after the birth of her child. The chief purpose of providing these tablets after the birth of the child is to help supply the nutritional requirements of breast-feeding mothers but they are also of benefit to all mothers of young children whether they are breast-feeding their child or not. The tablets were being supplied in addition to the free cod-liver oil supplied to the children. They were available at all Maternity and Child Welfare Centres and all mothers who had babies under thirty weeks old on 1st August, 1947, had to apply to their local food offices and were given coupons for tablets to last them until the baby was 30 weeks old. After 1st August, 1947, mothers were given these coupons automatically when they notified the food offices of the birth of a child. A similar scheme was found most useful by me in the year 1947 in Delhi railway area.

III. *House visits*

It must be realized by all concerned that in all civilized countries the precautionary measures for mothers and children have made great strides during the last twelve years. The idea that

children of to-day are the nation of to-morrow is being more and more realized. The war, pestilence and famine do cause a great havoc but at the same time thought of the future generation should receive great attention and new methods for the maintenance, particularly of the coming generation, should be thought of. It is the duty of the health visitor to visit the expectant mother in her home at the time of delivery and teach her on the spot the correct method of living during this period at and after delivery.

C. *OPENING NEW CENTRES ON CO-OPERATIVE BASIS*

Due to financial stringency, the Railway Administrations are not able to open new health centres. A scheme of voluntary contribution of one or two annas a month from each railway employee in the workshops (over 12,000 men are working in Kanchrapara Loco. and Carriage Workshops at present) is under consideration and is meeting with excellent response and it is hoped a Health Centre will be started at Kanchrapara in near future on co-operative basis. This may be done at other workshops too.

My thanks are due to Dr. S. S. Kent, M.D., Chief Medical Officer, E. I. R., for his kind permission to contribute this article.

NOTE ON DIET SURVEYS CARRIED OUT IN THE CENTRAL PROVINCES AND BERAR

By D. M. ROY

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1. DIET surveys were carried out among 10 poor families of the agricultural labourer class in the village of Rajakheri, district Saugor (wheat tract), over a period of 7 days during the month of December 1946. It was done by weighing method, from house-to-house visit, morning and evening every day. The intake of the various foods per consumption unit per day and the chemical composition of the average diet were found to be as follows (table I).

Comment.—The diet was adequate in calories owing to excessive consumption of cereals required to give full energy to the hard working labourers but it was grossly deficient in protective foods like milk and milk products, vegetables, fruit, meat, fish and eggs. It is noted that the chemical composition of the same average diet meets fairly the minimum daily requirement of total protein, calcium, iron, vitamins A, B and C. The total fat falls a little below the minimum requirements of 45 gm. as recommended in the *Health Bulletin* no. 23. We do not yet know the exact daily requirements of fat.

On the basis of this finding it is worth investigating further how a poor man's diet in

the village may not fall far below the recommended minimum for vitamins and minerals in areas where the poor man consumes more quantities of wheat in a mixture of other cereals, namely rice and juar with big quantities of pulses without adequate quantities of protective food. This vegetarian diet of course fell short of the recommended standard of *animal* protein though the total protein was more than the required minimum.

milk, fruit, meat, fish and eggs. The cereals consumed were predominantly millets. This diet was below the recommended minimum requirements as regards protein and fat but adequate as regards calcium, iron, vitamins A, B and C.

3. Diet surveys were carried out among 10 poor agricultural labourer families in the village of Abhanpur, district Raipur (rice tract), for a period of 7 days during the month of July 1948.

TABLE I

Item	Ounces per c.u. daily	Chemical composition	Per c.u. daily
Rice	9.6	Carbohydrate	951.0 gm.
Wheat	18.2	Protein, total	178.4 gm.
Juar	5.06	Protein, animal	1.7 gm.
Pulses	13.3	Fat, total	26.7 gm.
Leafy vegetables	2.0	Fat, animal	3.6 gm.
Non-leafy vegetables	0.99	Calcium	1.0 gm.
Ghee and butter	0.006	Iron	82.3 mg.
Vegetable oil	0.19	Vitamin A	5,352 I.U.
Meat and fish	<i>Nil</i>	Vitamin B ₁	1,808 I.U.
Eggs	<i>Nil</i>	Vitamin C	53.5 mg.
Milk and milk products	1.47		
Fruits	<i>Nil</i>		
Sugar or jaggery	0.44	Calories—	
		Gross	4,686
		Less 10 per cent (net)	4,218

2. Diet surveys were carried out among 10 aboriginal families (Koles) in the village of old Dindori, district Mandla, over a period of 7 days during the month of December 1946 by weighing method. This is an aboriginal tract where Baiga, Gond, Kole, and other aboriginal tribes live. The quantities of the various kinds of foodstuff per consumption unit per day and the chemical composition of the same were found to be as follows (table II).

Comments.—The diet is adequate in calories but deficient in protective foods like vegetables,

The intake of the various foods per consumption unit per day and the chemical composition of the same average diet were found to be as follows (table III).

Comments.—This diet was adequate in calories but deficient in fat, calcium, vitamins A and C. This diet contained very little protective foods like vegetables, fruit, milk, meat, fish and eggs.

4. Diet surveys were carried out among 10 poor families of the labourer class in the village of Dongargaon, district Drug, in the newly

TABLE II

Item	Ounces per c.u. daily	Chemical composition	Per c.u. daily
Juar	0.16	Protein, total	59.6 gm.
Rice	5.15	Protein, animal	Negligible
Wheat	5.51	Fat, total	19.5 gm.
Kudo	29.33	Fat, animal	Negligible
Maize	1.03	Calcium	0.67 gm.
Pulses	3.76	Iron	42.3 mg.
Leafy vegetables	4.69	Vitamin A	8,617 I.U.
Non-leafy vegetables	0.35	Vitamin B ₁	1,468 I.U.
Ghee and butter	0.001	Vitamin C	101.9 mg.
Vegetable oil	0.17		
Fruits	<i>Nil</i>		
Meat and fish	0.03	Calories—	
Eggs	<i>Nil</i>	Gross	4,183
Milk and milk products	<i>Nil</i>	Less 10 per cent (net)	3,765
Sugar or jaggery	<i>Nil</i>		
Condiments and spices	0.16		

TABLE III

Item	Ounces per c.u. daily	Chemical composition	Per c.u. daily
Rice	31.4	Carbohydrate	767.2 gm.
Wheat	<i>Nil</i>	Protein, vegetables	84.9 gm.
Juar	<i>Nil</i>	Protein, animal	Negligible
Pulses	3.2	Fat	18.7 gm.
Leafy vegetables	1.9	Calcium	0.33 gm.
Non-leafy vegetables	0.06	Iron	26.3 mg.
Fruits	<i>Nil</i>	Vitamin A	1,648 I.U.
Ghee and butter	<i>Nil</i>	Vitamin B	354 I.U.
Vegetable oil	0.47	Vitamin C	41.0 mg.
Milk and milk products	0.19		
Meat, fish and eggs	0.04		
Sugar or jaggery	0.01	Calories—	
		Gross	3,572
		Less 10 per cent (net)	3,215

TABLE IV

Item	Ounces per c.u. daily	Chemical composition	Per c.u. daily
Rice	30.1	Protein	99.8 gm.
Wheat	1.6	Fat	44.1 gm.
Pulses	4.8	Calcium	0.31 gm.
Green leafy vegetables	Negligible	Iron	25.5 mg.
Non-leafy vegetables	4.8	Vitamin A	530 I.U.
Ghee and butter	Negligible	Vitamin B ₁	575 I.U.
Vegetable oil	1.2	Vitamin C	48.0 mg.
Meat and fish	0.28		
Eggs	<i>Nil</i>		
Milk and milk products	1.2	Calories—	
Fruits	Negligible	Gross	4,109
Jaggery	1.02	Less 10 per cent (net)	3,699

merged Chhatisgarh State, over a period of 5 days during the month of September 1949. The intake of the various foods per consumption unit per day and the chemical composition of the average diet were found to be as follows (table IV).

Comments.—The average diet is adequate in calories but lack in protective foods like milk, green leafy vegetables, fruit, meat, fish and eggs. The diet is deficient in fat, calcium, vitamins A and C.

My grateful thanks to Lieut.-Colonel A. S. Garewal, I.M.S., for his kind permission to publish this article.

[The author has weighed the food in the house and refuses to admit that anything beyond that food was ever eaten. This, at least for an agricultural population, is not comprehensible. Sugarcane, maize cobs, roasted or raw gram pods, radishes, carrots, Indian plums, mangoes and many other vitamin-containing vegetables and fruits the labourers can and do help themselves to freely, out of doors. As a matter of fact, going by what is known about the Punjabs and Uttar Pradesh the poorer the villager, the better is his vitamin consumption.—EDITOR, I.M.G.]

USE OF DEFATTED GROUNDNUT CAKE FLOUR AS FOOD*

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Introductory

THE nutritive value of groundnut cake as cattle fodder has long been known. Boigey (1929) has reported good results with the groundnut cake flour fed particularly to children. This was used by him in various food preparations. Mitchell and Block (1946) have recommended that there must be a limit to the proportion of groundnut flour taken in daily diet. They

- *1. Supported by a grant from the Ministry of Health, Government of India.
- *2. A paper read at the 37th session of Indian Science Congress, Poona.

further report that cooking and methods of use are of primary importance. In Western countries the flour is mixed with other flours and used in soups, sauces, biscuits and bread. For ordinary bread and pastry it is said that the groundnut flour content should not exceed 10 per cent to 15 per cent. Schulz (1948) has reported the use of the flour in Germany, where it is mixed with wheat flour and made into bread.

In India groundnut by itself is consumed as snacks, but so far no attempt had been made to popularize the use of the defatted flour though it is rich in protein and vitamins. In view of the shortage of foodstuffs, other avenues are being explored to find out suitable substances to meet the shortage of proteins and vitamins in the national dietary. There is a consensus of opinion that groundnut could be incorporated in our daily diet. The groundnut by itself is very rich in fat and if consumed in large quantities is liable to produce digestive disturbances and as such before advocating its consumption it was decided to take up investigations on the following aspects of the problem :—

(a) The amount that could safely be included in the daily diet without detriment to health, and the extent to which it could safely replace cereals.

(b) The form in which it could be taken as pleasing and palatable article of food.

The present article deals with these two problems.

Methods

It was thought that as children are easily affected by change of diet experiments should be carried on them and children of Anjuman Khadimul Islamia Muslim Orphanage of Patna City were selected for the purpose. Samples of defatted groundnut cake flour for experimental purposes were very kindly supplied by the Swastika Oil Mills, Bombay, at the instance of Secretary, Food Production Committee, Ministry of Food, Government of India. The flour was of two types, with and without the red cuticle. Wheat was obtained through the Rationing Officer, Patna, sifted, cleaned and milled. The wheat flour was mixed with the two types of defatted groundnut cake flour in the proportion of 10, 15 and 20 per cent of each. To ensure thorough and uniform mixing, it was again passed through the mill. To ensure purity, the milling and mixing were done in presence of one of the authors.

An analysis of the groundnut cake flour was done in this laboratory. Table I gives the results of analysis.

Rancidity was tested according to the technique of B. S. I. (1938) and Dastur and Lea (1941).

The children of the orphanage ranging from 5 to 14 years in age were divided into four groups (A, B, C, D) by random grouping. Each group

TABLE I

Percentage composition of the defatted groundnut cake flour

Type of flour	Moisture	Sand and grit	Protein	Fat	Carbohydrate (by difference)	Rancidity
Red ..	10.3	0.6	48.5	8.2	32.4	Positive
White ..	10.6	0.5	49.2	8.1	31.6	Positive

consisted of 18 boys. The average age of each group was 7.8 years. They were all in good health and with no signs of any of the deficiency diseases. After 3 days of the start of experiment two of the boys from each group developed malarial fever and had to be dropped.

The defatted groundnut cake flour of both types was given to the batch of boys in the form of 'chappatis'† at 10, 15 and 20 per cent levels. Each of the boys was consuming on an average 13 oz. of the mixed flour and was getting 1.3, 1.95, and 2.6 oz. of the pure defatted groundnut cake flour per head per day. The 'chappatis' were prepared and fed in the presence of one of the authors.

The boys were allowed one week's rest, after which groups A, B and C were fed for a week on 'chappatis' made of wheat flour mixed with 10, 15 and 20 per cent of the white groundnut cake flour only. Each of the boys was consuming on the average 13 oz. of the mixture per day. Group D was fed on pure wheat flour only.

After the boys were given another week's rest groups A, B and C were fed at 10, 15 and 20 per cent of the white groundnut flour mixed with wheat flour made up as 'chappatis'. The average consumption per head per day was 7 oz. of the mixture which contained 0.7, 1.05 and 1.4 oz. of the pure white defatted groundnut cake flour.

In each of the above experiments the boys were fed for 7 days.

After the lapse of a week's rest two groups were given the two types of flour mixed in the pulses and vegetables as thickening agents. These were the only two methods in which it could be incorporated in their daily diet.

Besides the 'chappatis' they were consuming the articles of food as in table II during the period of experiment.

This was their daily routine consumption even in normal times, except for the rice. During the period of rest the boys were on the normal

† Flour is made into dough, spread as thin circular discs about 6 inches in diameter and baked on an iron flat pan, till cooked.

orphanage diet which consisted of rice and items in table II.

TABLE II

Consumption per head per day in oz.

Type of food	Frequency of consumption during a week	Average
Soaked fried grain ..	7	1.9
Gram as pulses ..	6	1.2
Colocasia ..	6	2.1
Jaggery ..	2	0.3
Potato and other vegetables ..	2	2.3
Beef ..	1	1.8

Results

Table III shows the results of the first experiment. The boys were given the 'chappati' meal both morning and evening. The figures

white flour did not show any marked difference in digestibility. The opinion of the boys except for one or two with regard to the taste and smell was good.

The boys were accustomed to take rice both morning and evening. Wheat used to be given to them on very rare occasions. In order to evaluate whether wheat by itself had any effect in upsetting their digestive system, the experiment was repeated on the same four groups after they were given a week's rest. Table IV shows the result of this experiment.

The number of symptom-free boys at 20 and 15 per cent levels was less than that in first experiment while there was no difference at 10 per cent level. The boys on pure wheat flour were symptom-free.

After the lapse of another week another set of experiment was planned and the boys were given one meal consisting of the mixture of wheat and white groundnut cake flour while the other meal was their usual rice diet. The total

TABLE III

Showing palatability and incidence of digestive disturbances amongst the boys

Percentage of groundnut cake flour	Total number of boys	Total number of symptom-free boys	Percentage	Diarrhoea only	Indigestion only	Opinion of boys for palatability	Total groundnut cake flour consumed per day per head in oz.
20 { White ..	16	12	75.0	3	1	Good	2.6
20 { Red ..	16	11	68.7	3	2	Good	2.6
15 { White ..	16	12	75.0	3	1	Good	1.95
15 { Red ..	16	12	75.0	2	2	Good	1.95
10 { White ..	16	14	87.5	1	1	Good	1.30
10 { Red ..	16	14	87.5	2	Nil	Good	1.30

TABLE IV

Showing digestibility and palatability of white groundnut cake flour as compared with wheat flour

Percentage of groundnut cake flour	Total number of boys	Total number of symptom-free boys	Percentage	Diarrhoea only	Indigestion only	Opinion of boys for palatability	Total groundnut cake flour consumed per day per head in oz.
20	16	10	62.5	4	2	Good	2.6
15	16	11	68.7	3	2	Good	1.95
10	16	14	87.5	1	1	Good	1.30
Pure wheat	16	16	100.0	Nil	Nil	Good	0.0

reveal that the percentage of boys showing no digestive disturbances increased with the lowering of the percentage of the defatted groundnut cake flour in the 'chappati'; and when they were consuming 1.3 oz. of the defatted groundnut cake flour in the 'chappati', there were 87.5 per cent who were symptom-free. The red and the

consumption of the mixed flour in a day per head was 7 oz. Table V shows the results and the amount of pure white defatted groundnut cake flour consumed by each boy per day.

When they were consuming 1.4 oz. of white groundnut cake flour, 93.7 per cent were symptom-free at 20 per cent. level, while none of them

TABLE V

Showing digestibility and palatability with lesser quantity of white groundnut cake flour

Percentage of groundnut cake flour	Total number of boys	Total number of symptom-free boys	Percentage	Diarrhoea only	Indigestion only	Opinion of boys for palatability	Total groundnut cake flour consumed per day per head in oz.
20	16	15	93.7	Nil	1	Good	1.40
15	16	16	100.0	Nil	Nil	Good	1.05
10	16	16	100.0	Nil	Nil	Good	0.70

showed any symptoms of digestive disturbances up to 1.05 oz. of groundnut cake flour per head per day.

The other ingredients of their meals throughout were the same as in table II. When the groundnut cake flour was given to the boys as a thickening agent for the vegetables and pulses, they all refused to take it because of the unpalatability of the dishes and the experiment had to be discontinued after 2 days. The quantity of groundnut cake flour consumed by each boy per day during this period varied from 1 to 2 oz.

The flour when administered in the form of sweets, the recipe of which is given below, was readily consumed.

Recipe for 'Halwa'

Bengal gram flour 32 oz.
White groundnut cake flour 8 oz.
Butter fat (ghee) 4 oz.
Jaggery 12 oz.

Method

The mixture of flours was first fried in the ghee and jaggery in water was added while on fire. The mixture was allowed to thicken.

The boys were examined every day by one of the authors for any evidence of deviation from the normal. All complaints were noted. With regard to the diarrhoea the maximum of loose stools was three times a day. None of the boys of any group showed any evidence of allergy to the groundnut protein.

Conclusion

When groundnut cake flour was given to the boys in the form of 'chappatis' at the different percentage level, they were found to exhibit signs and symptoms of digestive disturbances when both the principal meals consisted of the same.

The digestive disturbances were always of a mild nature and in no case the symptoms or signs assumed alarming proportions. The incidence of digestive disturbances was progressively lower with a lowering of the consumption of the defatted groundnut cake flour.

The boys were always accustomed to take rice in both their principal meals. Wheat for them

was always a rarity. In order to find out whether wheat by itself could produce digestive disturbances, another set of experiment was planned which showed results similar to the first with the difference that the number of symptom-free boys was less than in the first experiment while boys on the pure wheat flour remained symptom-free. The lesser number of symptom-free boys in the second experiment at 20 per cent and 15 per cent levels may be due to the fact that the boys had not completely recovered from their digestive upset created in the first experiment.

The third series of experiments showed that the flour could be administered safely to the extent of 1.05 oz. per head per day.

No significant difference in digestibility and palatability was observed between the red and white groundnut cake flour. The flour could not be made palatable for use as thickening agent for vegetables and pulses. It could, however, be made into palatable dishes with fat and sugar.

Summary

1. Batch of boys in good health were put on varying proportions of defatted groundnut cake flour with and without the cuticle.
2. They could digest the flour only up to 1.05 oz. a day and in this amount it could be given with safety.
3. There were no differences in the digestibility of red and white flour.
4. Flour was not palatable when used with pulses and vegetables.
5. Flour could be used in making sweet dishes.

I am grateful to Dr. K. Mitra of the Director-General of Health Services Office for kindly arranging for funds and the groundnut cake flour as also for his suggestions.

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The Indian Medical Gazette

Fifty Years Ago

CORRESPONDENCE

(From the *Indian Medical Gazette*, July 1900,
Vol. 35, p. 277)

THE HOMŒOPATHIC MEDICAL SCHOOL

To the Editor of 'The Indian Medical Gazette'.

DEAR SIR,—I enclose a 'cutting' from the *Statesman* of 1st June. I have no doubt that Lieutenant-Colonel K. P. Gupta's lecture on the 'Sanitary (should it not be insanitary?) condition of Bengal' will be both instructive and useful. Sanitation too is much the same for all sects of medical practitioners, so no fault can be found on the score of the subject chosen. The I.M.S., however, is not worked on *homœopathic* lines and a conscientious homœopath is a man for whom I cannot feel any respect at all. The absurdity of the doctrine when carried to its logical conclusion has been laid bare again and again, and I do not think it is at all becoming for Lieutenant-Colonel K. P. Gupta, I.M.S., to encourage the 'Homœopathic Medical School'. By what right does the 'Homœopathic Medical School' hold examinations and grant diplomas and degrees?

Yours, etc.,
F. L. S.

'Homœopathic Medical School.—This school has passed twenty-three Licentiates and a Bachelor in Medicine and Surgery. The classes open on 15th June, and the inaugural address on "Prevention of diseases, with special reference to the sanitary condition of Bengal" will be delivered by Colonel K. P. Gupta, I.M.S.—*Statesman*, 1st June, 1900'.

[We should say the so-called school had no right at all to grant diplomas, and it is certainly not at all right for an L.R.C.P. and L.R.C.S. of Edinburgh to preside at the meeting of such a school.—EDITOR, I.M.G.]

FILARIAL METAMORPHOSIS IN THE ANOPHELES

To the Editor of 'The Indian Medical Gazette'.

SIR,—Since I sent you off my article on filarial metamorphosis in the anopheles genus of mosquito (*Indian Medical Gazette*, May 1900), I have again worked out the metamorphosis in two batches of anopheles with the same results, but with the important addition that I have found the final stage of the filaria in the head

and actually partly within the proboscis of the mosquitoes. I am, therefore, now of opinion that infection during the act of 'biting' is the most probable way. My paper with details is being sent to the B. M. Association Meeting at Ipswich.

Yours, etc.,
S. P. JAMES,
CAPTAIN, I.M.S.

Quilon,
30th May, 1900.

A GARBLED QUOTATION

To the Editor of 'The Indian Medical Gazette'.

SIR,—In your issue of March 1900, page 95, Colonel Lawrie, I.M.S., writes as follows:—

'While the microscope possesses a certain scientific value in malaria, which is still indefinite, there is no doubt that it has acquired a very distinct commercial value in the profession; indeed Ross has gone so far as to state that "the success of Imperialism in the coming century will depend largely on the microscope in malaria", notwithstanding that the science of malarial parasitology has been proved to be founded almost exclusively on assumption and not on fact'.

In a footnote, Colonel Lawrie gives the *Times*, Tuesday, 28th November, 1899, page 11, as his authority for the above quotation from my lecture to the Liverpool Chamber of Commerce. I now enclose an extract from the *Times* to which Colonel Lawrie refers—the extract having been sent to me by the General Press Cutting Association. I also enclose a cutting from the *Liverpool Courier* for Tuesday, 28th November, giving my lecture in full. From both of these it will be seen that Colonel Lawrie has altered the passage which he quotes from my lecture. What the *Times* actually wrote was that: 'He (i.e. myself) believed that in the coming century the success of Imperialism would depend largely upon success with the microscope'—meaning, of course, on the microscopic investigation of disease. The *Liverpool Courier* gives the same passage in my own words. In neither paper do we find the smallest justification for the addition of the two words 'in malaria' which some one—I presume Colonel Lawrie—has thought fit to append to my utterance; there is no justification for them, either in my words themselves or in the context. The words could scarcely, I think, have been inserted by accident. I must assume then that they were put in, partly in order to make me out as having been the author of a ridiculous statement (namely, that Imperialism will depend on the microscope in malaria—that is, in the diagnosis of malaria!) and partly in support of Colonel Lawrie's

previous sentence which means—if it means anything—that the profession uses the microscope in malaria for commercial purposes—a delicate innuendo which will scarcely escape the reader.

I shall be much obliged if you will kindly publish this letter and endorse the correctness of my quotation from the *Times*.

Yours faithfully,

RONALD ROSS, D.P.H., M.R.C.S.

School of Tropical Medicine,
Thompson-Yates Laboratory,
University College,
Liverpool.
20th May, 1900.

[Dr. Ross' statement is correct. The words 'in malaria' are not found in the article in the *Times* of 28th November.—EDITOR, *I.M.G.*]

THE VALUE OF 'SAGS' AS ANTISCORBUTICS IN THE JAIL DIETARY

To the Editor of 'The Indian Medical Gazette'.

SIR,—In response to the invitation made by you in a footnote to Captain Jennings' letter in the June number of the *Indian Medical Gazette* asking for an expression of opinion by Medical Officers of Jails on the desirability of banishing 'sags' from the jail dietary, I should like to say that my opinion agrees with Captain Jennings so far as regards some of the better classes of indigenous vegetables of this nature.

'Cholai sag' referred to by him appears to be the name in use in the north-west provinces for the *Amaranthus anardana*, an ally of the *Amaranthus gangeticus* Linn., which is known in Chota Nagpur by the Santali name 'Gandhari sag' and more generally in Bengal as 'Lal sag'. This I consider the best of these vegetables by a long way but another commonly grown, the 'Palang' or 'Palki' sag (*Beta bengalensis*) is also good. There are other similar vegetables appreciated by the better class natives but for various reasons are unsuitable for growth in jail gardens. These two sags will grow at nearly all times of the year in the Hazaribagh district where European vegetables are unobtainable, and I think most Europeans at those times of the year occasionally eat and enjoy them. They cook very well and suit very well prisoners with a tendency to bowel disorders. Although I prefer to give to weakly prisoners mixtures of potatoes, onions, beet-root, etc., during the hot weather, yet I cannot think that sags of the above kinds are without antiscorbutic qualities, sufficient to warrant their general use with the ordinary classes of prisoners.

The disrepute into which this class of vegetable has fallen is due to the use of the leaves of a great variety of plants grown for other purposes, particularly the leaves of cucurbitaceous plants grown for their gourds and the leaves of potatoes, gram, etc. Many jailors are in the habit of making use of these articles to make up the required ration in times of difficulties. I consider the condemnation of such sags to be most proper.

With regard to the method of cooking, Captain Jennings says that in jails it is impossible to cook sags without using a large quantity of water and straining. In the Hazaribagh Central Jail, and I believe generally in Bengal jails, it is usual to cook all classes of vegetables with the exception of potatoes with the addition of but a very small quantity of water which is not thrown away. There appears to be no difficulty in doing this in large iron cooking vessels, the vegetable is cut up into small pieces and piled up in the cooking vessel, water is added only in sufficient quantity to prevent burning at the bottom; the water in the vegetables is sufficient to cook them well.

Experience in a question of this kind is no doubt apt to be fallacious as probably nowhere are these vegetables at all exclusively used. An analysis of the salts might throw more light on this subject, but I do not think the process described in Captain Jennings' letter is a sound one. It in no way determines the presence of the organic salts which are generally believed to be the constituent of vegetables which gives them their antiscorbutic value, for in the method described by him the salts found might have been almost exclusively lime and silica or inorganic soluble salts in their original form in the uncooked vegetables.

I am, etc.,

A. H. NOTT,

MAJOR, I.M.S.

Hazaribagh,
9th June, 1900.

Current Topics, Etc.

World Braille—An Advance Toward One World

By PERCY WINNER

UNESCO Staff Writer

(Reproduced from UNESCO Features, No. 19, 15th April, 1950, p. 10)

BLIND men and women who read with their fingertips are nearer the goal of an international script than people who use their eyes to read.

Scores of different languages in all parts of the earth are now read by the blind, but as the result of agreements reached at a ten-day meeting during March in

UNESCO House—the International Braille Conference—a single Braille system adaptable to all the world's languages—and to be known as World Braille—will be created. To bring this about, the conference recommended that a World Braille Council be established to work out the technical details.

World Braille will be based upon the original system of raised-character writing developed by the Frenchman Louis Braille, himself blind, more than a century ago. And in tribute to Braille, the conferees recommended that workers for the blind in all parts of the world observe his birthday as an annual holiday and that a world commemoration be arranged for the centenary of Braille's death in 1952.

As envisaged, World Braille will be a complete tactile representation of visual scripts, with the maximum degree of consistency among the Braille systems of the various language groups. Except where the complexities of ideographic scripts make it impossible a Braille symbol will be provided for each visual letter, with the understanding that the sound value of the symbol be identical with that of the visual letter of the alphabet of the particular language.

More than half of the delegates who attended the meeting were blind themselves. They came from countries as far apart as Brazil and India, from Pakistan, China, Egypt, Ceylon, England, Greece, the United States; and they included linguists, phoneticians, blind educationists and representatives of Braille printing houses.

This important milestone in the history of Braille was not reached without sacrifices in the common cause by various groups of Braille readers. Because of conflicting methods in adapting Braille in the past they will have to discard much of what they have learned—over periods of many years—and begin all over again. S. T. Dajani, Principal of the Alaiya School for the Blind, Ramallah, Hashemite Jordan, volunteered to scrap twelve years of hard work. A similar offer was made by C. K. Dassnasike, Principal of the School for the Blind, Mount Lavinia, Ceylon.

One of the achievements of the conference was an agreement to begin the formulation of a uniform Chinese Braille based on Mandarin, but retaining a considerable degree of sound relationships with traditional Braille. There are four main spoken forms of Chinese, of which the Pekin Braille code has 408 characters, and that of Union Mandarin has only 54 characters.

Dr. Helen Keller, world-famous American blind-deaf personality, in whose honour a special session of the conference was held, told delegates that through their work a new era for the blind was beginning, for, she said, they were 'lifting the blind throughout the world from age-long darkness into the light of culture and knowledge'. 'Through them and through UNESCO's activities on behalf of the blind', she added, 'the voice of the blind is being heard in words that are to be put into concrete assistance throughout a world of good will'.—UNESCO.

[For an account of this remarkable personality see this journal, vol. 84, page 15, January 1949.—EDITOR, I.M.G.]

The Oslo School Breakfast

By RUTH SACHS

Special UNESCO Writer

(Reproduced from UNESCO Features, No. 20, 1st May, 1950, p. 7)

MANY educators to-day label the new age dawning as 'Filiarchy—the age of the child'. This odd, new word reflects the growing and real respect in many countries for children as individuals, with the right to shape many aspects of their own lives. It is recog-

nized that the innate desire of the children to express themselves is a vital element in training them to become full and useful personalities.

One nation, Norway, has used the simple device of having its children breakfast together, as an important means for applying this principle and for helping young people to become well-balanced tolerant adults.

In Oslo, physicians joined with educators to find a good way of balancing the physical and emotional needs of children. As a means of starting the young child's life right, the experts decided that every day should start right. This was interpreted quite literally—and the Oslo School Breakfast is the result.

The simplicity of the menu barely reveals the considerable research from which it evolved. As a minimum, the Oslo children have for the first meal of the day one-half coarse brown roll, one slice of brown bread, both generously topped with butter and goats' milk cheese; one large bowl of milk; and either half a raw apple or a raw carrot. They can have second, third—or fourth—helpings of any or all of these dishes. Each of the factors of the meal has been studied and tested for maximum vitamin content, and is calculated to build strong muscles, teeth and bones.

Education and the meal, as well, are both compulsory and free. Breakfast is furnished free to all. All attend with gusto. Thus children of workers, of college professors, of embassy officials, of shopkeepers, of the Crown Prince and Princess, sit together at long tables, and break bread together—literally. Herein lies an important common denominator, a levelling factor, with a minimum of artificial social pressure, with no greed and no unsatisfied material need.

Since mothers in Norway are assured the full constituent of wholesome meals for their children in the school breakfast, they are not harassed by the necessity to prepare midday meals for their offspring. There is no lunch period, *per se*, in all of the Norwegian way of life. The fathers of these children end their office days at 4 p.m. in the winter, and 3 p.m. in the summer, and thus, close family ties are established—and maintained with relative ease.

Each of the groups of children, who enjoy the school breakfast, has forty full minutes in which to consume the meal. And the children actually eat for a full forty minutes. They neither dawdle nor grab; they do not whimper nor whine. Five hundred youngsters file into the dining-room in orderly procession. They are not supervised, nor are they issued orders, they know this is breakfast, at leisure.

Their approach to the food set before them is like that of adults at a party. Unhurriedly they unwrap their sandwiches, and munch with great deliberation. No one stands over them to prod or hurry. They speak calmly with their neighbours. Their conversation bespeaks the placidity of their entire way of life.

One small girl spies the writer observing them. She smiles shyly and nudges her companion. Soon many eyes view the stranger. With sweet simplicity, the children ask questions: 'Where are you from? What is it like there? It must be wonderful to come from so far away. Do you have children? What are the children in your country like? Do they look like us?'

Word spreads that a foreign visitor is observing. The boys look frankly and curiously at the visitor. They hesitate at first to give voice, then: 'My father was in a foreign country, he was in the war, a soldier. . . . Tell us about baseball in your country'. One boy affectionately places his arm around his neighbour and offers: 'You ought to see Anton ski, he is the champion of our class'.

Thus with naturalness and no prompting, the children put the stranger at ease. They find no indication to shout, nor need to rush. Very few crumbs are left over, though the children can have as much of the food as they wish. Often the teenagers eat as much as a dozen slices of bread at a single sitting.

These children have forty daily minutes to share youthful hopes and ambitions and dreams; to match good table manners; to form lasting friendships; to balance the faster paced and the slower; to consume food companionably without discord or friction! Forty minutes of utterly relaxed freedom, perchance to ease the emotional strains of home-life!

There are no strictures, no admonitions delivered to the children during the meal. Sedately and unobtrusively walking about is one adult, to whom the children call friendly and pleasant greetings. The Supervisor is amiable and kind, showing genuine friendliness and interest in the pupils. She seems to remember all their names, and asks for the members of their families. Lest one think that five hundred children in one room might produce a deafening din, only the soft sounds of modulated happy voices reach the ear, and the cadence of blended soft voices resounds melodiously.

It is easy to see that these children are neither over-disciplined, nor frustrated, for they receive guidance, understanding, love and security, in the freedom of the Oslo School Breakfast.

Thus are the habits of the young formed, in peace and in harmony. No one pays less or more. No one pays at all. For the rich and the poor and the middle-class partake of the same fare and cast no overt glances up or down. There is freedom from want, and freedom from greed, established from young childhood to adulthood. Companionship with equal age-groups is assured, even for the offspring of one-child families.

Calm strength and strong-mindedness is their heritage. For they learn so very young and by bright example, the good and healthy way of living together in peace and harmony.—UNESCO.

Earth Growing Warmer, Not Colder, Urey Says

(From *Chemistry and Chemical Engineering in the United States*, dated March 1950, prepared by the American Chemical Society)

RADIOACTIVITY, which man has now begun to harness for his own use, was largely responsible for the development of the earth as we know it, according to a new theory of the planet's origin which was described by Dr. Harold C. Urey, Nobel Prize-winning chemist of the University of Chicago Institute for Nuclear Studies, Chicago, Illinois, at the Fifth Annual Southwest Regional Meeting of the American Chemical Society.

Dr. Urey suggested that heat generated by radioactive materials in the heart of an ocean-covered earth brought about vast structural changes which gave us the great land masses on which we live to-day.

The hypothesis outlined by Dr. Urey differs radically from the view, widely held in the past, that the earth was formed at a very high temperature and has been cooling off ever since. On the contrary, according to the new theory, the earth has grown warmer since it 'accumulated' some two billion years ago from a huge dust cloud which the sun had acquired during its travels through space.

At the start, Dr. Urey said, the earth probably consisted of a low-density core, followed by a layer of a mixture of iron and stone, and on the surface a very thin layer of rock. Covering the whole was a layer of water.

During the first stage of the earth's history, radioactive uranium, thorium, and potassium in the stony regions raised its temperature until the iron layer melted. Then the iron dropped to the centre of the globe, forming a heavy, dense core, which displaced the lighter materials originally there and floated them up to the surface. It was thus that the continental

land masses and the deep Pacific basin were formed, he explained. There probably was only a single continent for a time, according to the theory, but as material kept coming up from the earth's core and spreading out near the surface it broke this continent up and carried the sections apart. This idea fits in with the continental drift theory, advocates of which have noted that the eastern coast of the New World looks as if it had been split from the western coast of the Old World.

The following 4 items are reproduced from *Pharmacy in the United States*, dated March 1950, prepared by the American Pharmaceutical Association:—

Adsorption of Aureomycin by Aluminum Hydroxide Gel

F. E. DI GANGI and C. H. ROGERS (*Journal of the American Pharmaceutical Association*, Scientific Edition, **38**, 646, 1949) found that aluminum hydroxide gel has a high adsorption affinity for aureomycin, and this explains the low blood levels of aureomycin that have been observed clinically when aluminum hydroxide was administered simultaneously. The authors treated several solutions of aureomycin hydrochloride with the aluminum gel and after two hours assayed for potency both colorimetrically and bacteriologically, and they found that there was almost complete removal of aureomycin from the solutions. This constitutes further evidence against the use of aluminum hydroxide gel to prevent gastrointestinal disturbances from oral administration of aureomycin hydrochloride.

An Incompatibility Between Vitamin B₁₂ and Ascorbic Acid

A FIFTY per cent reduction in potency of vitamin B₁₂ ampoules containing ascorbic acid was noted after twenty-four hours' standing at 28-30°. W. C. Gakenheimer and B. A. Feller (*Journal of the American Pharmaceutical Association*, Scientific Edition, **38**, 660, 1949) prepared a series of ampoules with and without ascorbic acid and discovered that as little as 10 mg./cc. of ascorbic acid was sufficient to cause loss of more than half the potency of a solution containing 15 microgrammes B₁₂/cc.

A Colorimetric Assay for Antihistamines

A COLORIMETRIC method for the determination of the antihistaminic drugs containing the N(2-pyridyl) group was developed by H. M. Jones and E. S. Body (*Journal of the American Pharmaceutical Association*, Scientific Edition, **38**, 579, 1949). These workers treated a solution of the drug with cyanogen bromide solution and subsequently with aniline solution to develop a stable color which could be measured in a photo-electric colorimeter. The method was successfully applied also to the estimation of these drugs in urine, and the urinary excretion curve for tripeleennamine was determined. At present, the following drugs in wide use in the United States may be determined by this new procedure: tripeleennamine, thenylpyramine, methapyrilene, pyranisamine, prophenpyridamine and doxylamine.

New Antacids—Aluminum Glutamates

J. W. LEMAISTRE, J. M. HOLBERT, and I. W. GROTE (*Journal of the American Pharmaceutical Association*, Scientific Edition, **38**, 595, 1949) prepared a series of

basic aluminum salts of glutamic acid and found that they possess a capability of rapid neutralization and yet had a prolonged buffering action. The three new salts were dihydroxyaluminum sodium glutamate, tetrahydroxydialuminum magnesium diglutamate, and tetrahydroxydialuminum glutamate. It is suggested that they might be worthy of clinical tests as buffers to be used in hyperacidity.

Sterilization of Clinical Thermometers

(From the *Journal of the American Medical Association*, Vol. 141, 24th December, 1949, p. 1272)

THE majority of pathogenic micro-organisms which would be transmitted by oral thermometers are sensitive to the action of isopropyl alcohol (full strength), ethyl alcohol (70 per cent by weight) and propylene glycol (full strength). Propylene glycol has the advantage of being the least volatile. Thermometers infected with mycobacterium tuberculosis should be immersed in a 5 per cent solution of cresol and thoroughly rinsed before use. None of these agents is sporicidal.

Rectal thermometers cannot safely be disinfected by these agents. Immersion in sulphuric acid-chromate cleaning solution, followed by a thorough rinse prior to use, is probably the only certain method for their disinfection. If this procedure is not practical, 5 per cent cresol solution, followed by thorough rinse, may be substituted.

The efficacy of all disinfectants is reduced by organic matter; therefore, a mechanical cleansing is recommended before the thermometer is placed in solutions of disinfectants. Utilization of individual thermometers is advocated when practicable.

Epidemic of Cave-Borne Pulmonary Infiltrations with Eosinophilia

(From the *Journal of the American Medical Association*, Vol. 141, 24th December, 1949, p. 1259)

At a meeting of the Israel Medical Association in July 1949, W. Alkan spoke on an epidemic of cave-borne pulmonary infiltrations with blood eosinophilia. In October and November 1948, 40 cases of a feverish disease with high levels of eosinophils in the blood was observed in a Jerusalem army hospital. All patients reported that they had worked in an underground tunnel between two and forty-five hours.

The first symptoms, such as fever, cough and general fatigue, appeared five to eight days after the work in the tunnel had been completed. The fever lasted one to twelve days. Characteristic in the development of the disease was the involvement of the upper part of the respiratory tract with dry, frequent cough, sometimes with blood-stained sputum. In some cases nightly attacks of asthma occurred. Contrary to the severe clinical symptoms, there were few objective findings in the lungs, consisting mostly in single râles. Roentgen examination revealed often signs of interstitial pneumonia of a transitory character. Re-examination after four or five days did not show the infiltration.

Apart from the characteristic roentgen observations of the lungs, the constant, high level of eosinophils in the blood was remarkable, most cases showing a high leukocyte count, up to 26,700 per cubic millimeter, with a shift to the left. Between the fifth and thirteenth days the eosinophil count could be

determined absolutely (up to 12,200 per cubic millimeter and relatively up to 70 per cent of the total leukocytes). In the course of the disease the values of the eosinophilic cells in the blood varied. In some cases, increased values could be found for several months. Results of all other chemical and biologic tests remained negative.

The classic forms of the Loeffler syndrome have been observed and described several times in Israel. In 1944 the endemic appearance of a feverish disease with blood eosinophilia was reported in an Arab village near Haifa. The cause of this disease could not be ascertained. A year later the appearance of calabar-like swellings with a high eosinophil level was observed throughout the country. The disease was called eosinophilic erythredema (Steinitz, Lefkowitz and Kopstock).

The disease described herein is different from the Loeffler syndrome and Weingarten's 'tropical eosinophilia'. The latter has occurred so far only in India, the Pacific and in Africa. It is associated with leukocytosis, in 50 per cent with enlargement of the spleen and frequently with a positive cold agglutination. It responds well to treatment with arsenicals. The disease, as described in Israel, showed a negative cold agglutination in all cases and did not react to arsenicals altogether.

As none of the cases was fatal, no histologic examinations could be performed, and it could not be decided whether the changes in the lungs were of a peribronchial type (Weingarten) or peribronchial and perivascular damage (Loeffler).

Auscultatory Respiratory Murmur

(From the *Journal of the American Medical Association*, Vol. 141, 24th December, 1949, p. 1238)

For more than a century, auscultation has been one of the most important measures in the physical diagnosis of diseases of the lungs and pleura. However, often it is inadequate and disappointing, perhaps because of failure to teach properly its value. As a result it has often been replaced by roentgenography. Satisfactory physical examination should be an invaluable procedure. A new appraisal of auscultation, which is based on clinical experience and facts in physics and physiology discovered since Laennec's time, is claimed to show that the respiratory murmur is composed of sound vibrations originating in all component parts of the respiratory mechanism. It is now maintained that the respiratory murmur cannot be caused by air rushing through the larynx and impinging on the bronchial walls and dilating the air cells because the lungs always contain residual air which stops the force of the incoming current and causes the air to enter the finer bronchi and air cells by diffusion. The sound vibrations causing the vesicular murmur are said to originate in the respiratory mechanism in the anterior, lateral and lower portions of the thorax, where the air cells predominate, the musculature is light and the bony cage is elastic. That part of the respiratory mechanism which normally causes the bronchial murmur is found in the superior portion of the thorax and is most distinct posteriorly. Here the sound vibrations are produced by the air current, the larger bronchi, a comparatively small amount of pulmonary tissue and air cells, a heavy musculature and the least elastic portion of the bony cage. Thus once again studious and patient reevaluation of an important diagnostic procedure has revealed more modern interpretation of its mechanism but at the same time has re-emphasized its importance. Once again, thorough physical examination is shown to be of paramount importance and should not be replaced by 'logical substitutes'.

JULY, 1950]

Reviews

VITAMIN A REQUIREMENT OF HUMAN ADULTS
(M.R.C. SPECIAL REPORT SERIES NO. 264),
1949. Published by His Majesty's Stationery
Office, London. Pp. 142. Illustrated. Price, 3s.

THIS study was made in response to a request from the Ministry of Food for information on the adult requirement of vitamin A or its precursor, carotene, and was planned and controlled by the M.R.C. sub-committee on vitamin A and associate workers. Twenty men and three women volunteered for the experiment which last 2 years. During the first 8 months there was no noticeable change in the 16 volunteers kept on vitamin A free diet except a marked fall in the plasma-carotenoids. (The remaining 7 were on the same diet but received a prophylactic supplement of vitamin A or carotene.) Later, the vitamin A level of the plasma gradually began to decline. This showed great variation and only in 4 men did the fall become especially marked. With regard to the capacity for dark adaptation, which is the other criterion for vitamin A deficiency, there was deterioration during the winter months, after which it improved for no apparent reason, but unmistakable decrease in efficiency was observed in 3 out of the 4 subjects with very low plasma vitamin A. So judging by these criteria no more than 3 men could be judged certainly deficient, although several of the volunteers persisted with the diet for more than 18 months and one over 2 years. Other abnormalities such as follicular hyperkeratosis, conjunctivitis or undue fatigue commonly thought to be associated with vitamin A deficiency were either absent or equally present in both groups or present in the same subjects before and after depletion. Two cases of tuberculosis occurred among the volunteers, but it was not possible to determine whether the occurrence was more than a coincidence. On the available evidence from the curative and prophylactic tests, the daily requirement for healthy persons of pre-formed vitamin A is assessed as 2,500 i.u. and of carotene of various forms as about 7,500 i.u. When carotene is given in the form of vegetables, however, allowances must be made for inefficient absorption from the intestines.

That there should be delay in the appearance of symptoms is understandable from the fact that the healthy livers contain large vitamin A reserves, but what is surprising is the failure of these manifestations to appear in some of the volunteers. It may be that in typical vitamin A deficiency there are other factors at work besides the low intake of the vitamin, viz, chronic deprivation over many years, additional shortcomings in the diet or environmental factors. The report makes it clear that the results of the experiment are applicable to young adults and not to children, pregnant or nursing mothers or the chronically undernourished. There is room therefore for further research. Interested workers in this field will find in this monograph detailed descriptions of experimental technique and apparatus and of the painstaking manner in which the long and elaborate investigation was carried out.

R. N. C.

THE EYE MANIFESTATIONS OF INTERNAL DISEASES.—By I. S. Tassman, M.D. Second Edition. 1946. The C. V. Mosby Company, St. Louis. Pp. 614 with 243 illustrations including 24 in colour.

THE book describes the manifestations of internal disease as they occur in the eye. The first few chapters provide a description of the normal structure of the eye, general causes of the ocular lesions and methods of examination. Two chapters are devoted to structural

abnormalities and basic lesions of the individual structures of the eye. The succeeding chapters deal with the eye manifestations of various diseases—congenital, infectious, cardiovascular, blood, nervous, nutritional, etc. The important features of the ocular condition are described together with diagnosis and treatment. In this edition some new diseases and new illustrations have been added and the book has been revised up to date. Ophthalmology is an important branch of medicine and in many instances the ocular manifestations appear early in the course of the disease and are often of great diagnostic and prognostic significance. This lends importance to this book which is comprehensive and written in a simple style.

R. N. C.

TEXTBOOK OF HISTOLOGY.—By Alexander A. Maximow and William Bloom. Fifth Edition. 1948. W. B. Saunders Company, Philadelphia and London. Pp. xi plus 700 with 562 illustrations, 32 in colour. Price, 42s.

THE fifth edition of this book appeared in 1948.

The book was planned by Professor A. A. Maximow before his death in 1928. It was completed and edited by Professor W. Bloom in 1930.

The presentation of the subject by two anatomists follows the line of description of the hard facts of anatomy and leaves no room for doubt. The negative findings are plainly stated: 'Two types of mature human sperms containing either X or Y chromosome have not been described morphologically'. The genital systems, however, are dealt with very fully. Original photomicrographs are available on the implantation of the ovum and of human spermatozoa showing 48 chromosomes, including

Reconstruction diagrams are a feature. Among them the 'Portion of a pulmonary lobule' is probably the best.

Controversial topics like the monocytes have been given the space due to them. Incidentally in this account a misprint attracts attention (on page 47 the page referred to as 000 should be 108).

The get-up is superb.

An excellent publication.

S. D. S. G.

PATHOLOGY.—Edited by W. A. D. Anderson, M.A., M.D., F.A.C.P. 1948. The C. V. Mosby Co., St. Louis. Pp. 1453 plus xii with 1,183 illustrations and 10 colour plates. Price, \$15

THIS encyclopædic book on pathology is the work of 32 pathologists balanced and harmonized by the editor who has himself contributed 10 chapters out of a total of 46.

The topics covered include many which are not usually found in books on pathology. Instances are: (1) Wound producing capacity of moving bodies. The force in a simple forward motion may be computed by the formula $MV^2/2g$ where M equals weight in pounds, V the velocity in feet per second and g the acceleration of gravity or 32 feet per second—p. 128. (2) Heating effect of the electric current is calculated by $H = C^2R/4.187$ in which H is gram-calories per second, C is current in amperes and R is the resistance in ohms—p. 148. This occurs before one comes to: (3) The effects of radiation and horrors of Hiroshima and Nagasaki. 'Survivors in the Japanese cities described an instantaneous blinding flash of white or green light, accompanied by intense heat and preceding the shock wave of detonation. The mechanical blast was responsible for demolishing most of the houses in the cities and was forceful enough to break windows at a distance of 10 miles. The flash, of course, was electro-magnetic radiation in the visible range and the heat was due to a large component of infra red with some probable contribution from ultra-violet and visible rays. . . . The intensity and penetration of the

1 ounce of water) and taken early in the morning on empty stomach. This treatment may be repeated after 10 days if necessary. Meanwhile for local irritation in the perineum, an ointment of ammoniate of mercury (gr. 10 to one ounce of vaseline) should be used every night before retiring. Lack of personal hygiene is often responsible for reinfection.—N. V. B.

Re: stammering. The child may be sent to reside in India where the language is entirely different. Probably the stammering will cease in this new language.—Editor, I.M.G.]

PHYSICAL THERAPY JOURNALS

SIR,—Kindly let me have the full addresses of the following:—

1. American Journal of Electrotherapeutics.
2. American Journal of Physical Therapy.
3. British Journal of Physical Medicine.
4. British Journal of Actinotherapy.

GADARWARA,
(C. P.).

Yours faithfully,
S. S. BHATT, L.M.P.

- [1. American Journal of Electrotherapeutics and Radiology. Continued as Physical Therapeutics. 416 E., Market Street, Elmira, New York.

2. American Journal of Physical Therapy. 5N, Wabash Avenue, Chicago.

3. British Journal of Physical Medicine and Industrial Hygiene.

Butterworth and Co., Ltd., 4-6, Bell Yard, Temple Bar, London, W.C.2.

4. British Journal of Actinotherapy. Continued as British Journal of Physical Medicine from Vol. 6, 1931-32.

Butterworth and Co., Ltd., 4-6, Bell Yard, Temple Bar, London, W.C.2.

—EDITOR, I.M.G.]

Service Notes

APPOINTMENTS AND TRANSFERS

On return from leave Lieutenant-Colonel M. K. Kelavkar resumed charge of the post of Drugs Controller, India, with effect from the 5th April, 1950.

On return from deputation abroad Lieutenant-Colonel Barkat Narain resumed charge of the post of Director of Health Services, Delhi State, with effect from the 12th April, 1950.

Lieutenant-Colonel C. K. Lakshmanan is re-appointed as Director, All-India Institute of Hygiene and Public Health, Calcutta, with effect from the 17th April, 1950.

On relief by Lieutenant-Colonel Barkat Narain, Major M. S. Chadha resumed charge of the post of Deputy Director of Health Services, Delhi State, with effect from the 12th April, 1950.

Dr. G. S. Chopra, Deputy Assistant Director-General (Medical Stores), Medical Store Depot, Madras, was on deputation to Hyderabad Government on foreign service, with effect from the 25th October, 1949, to the 27th January, 1950.

On relief by Major M. S. Chadha, Dr. H. L. Malhotra resumed charge of the post of Assistant Director of Health Services, Delhi State, with effect from the 12th April, 1950.

On return from leave, Dr. A. K. Thomas, Officiating Medical Assistant, Central Research Institute, Kasauli, resumed charge of his duties at the Institute on the 13th April, 1950.

Dr. K. C. Virmani has been appointed as Staff Surgeon, Irwin Hospital, New Delhi, on probation for a period of 8 months, with effect from the 2nd May, 1950.

Mr. P. M. Nabar, Chief (Advisory Chemist in the Directorate General of Health Services, is appointed to officiate as Drugs Controller, India, with effect from the afternoon of 29th April, 1950.

LEAVE

Lieutenant-Colonel M. K. Kelavkar, Drugs Controller, India, is granted leave on average pay for 4 months, with effect from the afternoon of the 29th April, 1950.

Dr. A. K. Thomas, Officiating Medical Assistant, Central Research Institute, Kasauli, was granted earned leave for 30 days with effect from the 6th March to 4th April, 1950, followed by extraordinary leave for 8 days from the 5th to 12th April, 1950.

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CONTENTS

ORIGINAL ARTICLES

- Empyema Necessitatis following Closed Intrapleural Pneumonolysis with a Case Report.** By H. B. Dingley, B.Sc., M.B., B.S., T.D.D. .. 337

- Cutaneous Amœbiasis. With a case report.** By S. M. Ghosh, M.B. (Cal.), F.R.C.S. (Eng.), and Anjali Mukherji, M.B. (Cal.) .. 339

- The Relationship of the Body-weight to the Weights of the Organs. The Brain.** By P. V. Gharpure, M.D., D.T.M. & H., and H. I. Jhala, M.D., F.C.P.S., D.T.M. 342

- Epidemic Dropsy. A new test for argemone oil.** By R. N. Chakravarti, R. N. Chaudhuri and N. K. Chakravarty 344

CORRIGENDA .. 345

A MIRROR OF HOSPITAL PRACTICE

- A Case of Submucous Fibroid Simulating Pregnancy.** By K. P. Bhadury, M.B. .. 345

EDITORIAL

- Leprosy Tamed** .. 347

SPECIAL ARTICLE

- The Present Status of Sulphones in the Treatment of Leprosy.** By Dharmendra, M.B., B.S., D.B. .. 348

MEDICAL NEWS

- PAN-AMERICAN SANITARY BUREAU SENDS TYPHUS VACCINE TO AFGHANISTAN** .. 361

- W.H.O. TO SPONSOR INTERNATIONAL SYPHILIS SEMINARS IN HELSINKI AND PARIS NEXT SEPTEMBER** .. 361

- PAN-AMERICAN SANITARY BUREAU OFFICIAL CONFERS WITH HEALTH AUTHORITIES IN SOUTH AMERICA** .. 361

	Page
BRAZIL'S SNAKE FARM. By Arthur R. Pastore, Jr.	361
SEVENTIETH BIRTHDAY OF DR. HELEN KELLER	362
UTTAR PRADESH MEDICAL COUNCIL ..	362
BOMBAY MEDICAL UNION ..	363
LINSEED STRAW TO REPLACE JUTE ..	363
GROUNDNUT HUSK AS CATTLE FODDER ..	363
MEDICINE SPOONS ..	363
INDONESIA LAUNCHES VAST YAWS-CONTROL PROJECT	364
BEVAN TO VISIT INDIA AT EARLIEST OPPORTUNITY	364
PROFESSOR W. SCHUFFNER ..	364
OBITUARIES OF PHYSICIANS IN THE U.S.A. IN 1949	365
DRUGS RULES, 1945 ..	365
NOTIFICATION .. .	365
Indian Medical Forum ..	365
Domus Chirurgica ..	365
The Journal of Bone and Joint Surgery	366
THE NOBEL FESTIVAL ..	366
CONTROL OF SYPHILIS ..	366
\$52,320 (RS. 2½ LAKHS) GRANTED BY W.H.O. FOR MEDICAL SUPPLIES TO S.-E. ASIAN COUNTRIES ..	367
QUARANTINE RESTRICTIONS ..	367
NITROGEN MUSTARD HYDROCHLORIDE ..	367
RE.: THE UTRECHT FAIR, 1950 ..	367

(Continued on page 336)

CONTENTS—(Continued from page 335)

	Page		Page
FIFTY YEARS AGO		INDIAN CURDS OR 'Dahi' AS A SOURCE OF VITAMIN B COMPLEX AND GROWTH FACTORS. By N. V. Joshi (<i>Indian Journal of Medical Sciences</i> , Vol. 4, February 1950, p. 81)	376
OUR SPECIAL NUMBER (<i>Indian Medical Gazette</i> , August 1900, Vol. 35, p. 321) ..	368	PLASMA PROTEIN LEVELS OF HEALTHY INDIAN SUBJECTS. By G. N. Gokhale and R. G. Chitre (<i>Indian Journal of Medical Sciences</i> , Vol. 4, February 1950, p. 48)	377
CURRENT TOPICS, ETC.		A CASE OF SEVERE GENERALIZED REACTION TO MOSQUITO BITES. By W. Crewe and B. G. Maegraith (<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i> , Vol. 42, January 1949, p. 317) ..	377
CLINICAL EVALUATION OF VARIOUS TESTS FOR OCCULT BLOOD IN THE FÆCES. By S. O. Hoerr et al. (<i>Journal of the American Medical Association</i> , Vol. 141, 24th December, 1949, p. 1213) ..	369	MANAGEMENT OF ANURIA. By A. Miller (<i>British Journal of Urology</i> , Vol. 21, September 1949, p. 243)	377
MELANA : A STUDY OF UNDERLYING CAUSES. By H. L. Thompson and D. W. McGuffin (<i>Journal of the American Medical Association</i> , Vol. 141, 24th December, 1949, p. 1208)	369	HISTOPLASMOSIS AND TUBERCULOSIS (<i>Medical Officer</i> , Vol. 83, 21st January, 1950, p. 25)	378
RELATION OF RELAPSES IN TYPHOID TO DURATION OF CHLORAMPHENICOL THERAPY (<i>Journal of Tropical Medicine and Hygiene</i> , Vol. 53, January 1950, p. 21) ..	370	REVIEWS	
EXPERIMENTAL WORK WITH THE SULPHONE GROUP IN LEPROSY (<i>Journal of Tropical Medicine and Hygiene</i> , Vol. 53, January 1950, p. 16)	370	SYPHILIS : ITS COURSE AND MANAGEMENT. By E. W. Thomas, M.D. 1949	379
THIOARSENITES IN ANGEBIASIS : A CLINICAL APPRAISAL OF NEW ANGEBAIDES (<i>Journal of Tropical Medicine and Hygiene</i> , Vol. 53, January 1950, p. 19)	373	FUNDAMENTALS OF INORGANIC, ORGANIC AND BIOLOGICAL CHEMISTRY. By Joseph I. Routh, Ph.D. Second Edition. 1949 ..	379
A SIMPLIFIED PROCEDURE FOR BLOOD CELL COUNTS AND HÆMOGLOBIN DETERMINATION (<i>Physician's Bulletin</i> , Vol. 14, November-December 1949, p. 179)	374	LECTURES ON MEDICINE TO NURSES. By A. E. Clark-Kennedy, M.D., F.R.C.P. With a Foreword by Miss Clare Alexander. 1950	379
THE ACTION OF MERCURIAL DIURETICS IN CONGESTIVE CARDIAC HEART FAILURE (<i>Medical Journal of Australia</i> , Vol. II, 17th December, 1949, p. 888)	374	TUBERCULOSIS : A DISCUSSION OF PHTHISIOGENESIS, IMMUNOLOGY, PATHOLOGIC PHYSIOLOGY, DIAGNOSIS AND TREATMENT. By Francis M. Pottenger, A.M., M.D., LL.D., F.A.C.P. 1948	379
MANAGEMENT OF THE SYMPTOM COMPLEX IN ACUTE POLIOMYELITIS	375	ARTIFICIAL PNEUMOTHORAX IN PULMONARY TUBERCULOSIS. By T. G. Heaton, M.B. (Tor.). Second Edition. 1947	379
MEASLES ENCEPHALITIS : STUDY OF 50 CASES	375	MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS. PARTS I AND II. WRITTEN IN BENGALI. By Dr. Jotindra Nath Ghosal, L.M.S. 1356 B.S. (1949)	380
ERYTHROBLASTOSIS FÆTALIS. V. THE VALUE OF BLOOD FROM FEMALE DONORS FOR EXCHANGE TRANSFUSION	376	ERRATA	380
A STUDY OF THE EFFECTS OF MALARIA AND OF MALARIA CONTROL MEASURES ON POPULATION AND VITAL STATISTICS IN KANARA AND DHARWAR DISTRICTS AS COMPARED WITH THE REST OF THE PROVINCE OF BOMBAY. By D. K. Viswanathan (<i>Indian Journal of Malariology</i> , Vol. 3, March 1949, p. 69)	376	BOOKS RECEIVED	380
		CORRESPONDENCE	
		KALA-AZAR IN INDIA AND THE SANDFLY	380
		AUREOMYCIN IN KALA-AZAR	384

Original Articles

EMPHYEMA NECESSITATIS FOLLOWING CLOSED INTRAPLEURAL PNEUMONOLYSIS WITH A CASE REPORT

By H. B. DINGLEY, B.Sc., M.B., B.S., T.D.D.

Second Senior Assistant, Lady Lillithgow Sanatorium, Kasauli (Simla Hills)

ALMOST all cases of pulmonary tuberculosis having artificial pneumothorax treatment, unilateral or bilateral, require closed intrapleural pneumonolysis to improve upon the extent of the pulmonary collapse, though there is some diversity of views regarding its absolute indications and contra-indications. Some workers do not consider it as an essential procedure where the sputum is negative and cavity is apparently closed, while others are of the opinion that all cases having artificial pneumothorax treatment should have a trial of thoracoscopy and cauterization, if need be, irrespective of the fact whether adhesions are seen or not in the skiagram. According to them, all adhesions are not always visualized by radiological examination. The latest trend is that wherever adhesions are preventing an adequate collapse of the diseased focus, or are situated over the diseased focus, closed intrapleural pneumonolysis should be done irrespective of

- (1) whether A.F.B. are present or not in the sputum, and
- (2) whether the cavity is closed or patent.

This has been based on the observation of various workers, according to whom, lesions of the lung parenchyma, when there are no adhesions, not only heal better, but quicker than when A.P. is being maintained in the presence of adhesions. By severing the adhesion and releasing the lung from the chest wall we are avoiding respiratory trauma (Monaldi). The actual procedure is not completely devoid of various complications, of which the most frequent and simplest is surgical emphysema, the more serious being coagulation necrosis of the visceral stump leading to spontaneous pneumothorax with empyema. The other complications frequently met with, are pleural effusions, and internal hemorrhage from the intercostal vessels, as a result of injury to the neighbouring vessels or from the lung parenchyma.

A rare occurrence which was met with in one of our cases following closed intrapleural pneumonolysis was the occurrence of empyema necessitatis at the site of the puncture wound.

Case report

U. S., aged 25 years, male, transferred to this institution on 5th April, 1949, from Military Hospital, Dehra Dun.

The patient was having slight rise of temperature up to 99°F., cough with expectoration and was on artificial pneumothorax treatment (right).

History of present illness.—While on active service, in the month of October 1948, the patient started getting temperature up to 101°F. Later, cough started with slight expectoration and blood-stained sputum. Admitted to Military Hospital where skiagram of the chest was taken, which revealed exudative type of lesion with a cavity in the right upper and mid zone. Sputum on examination was positive for A.F.B., diagnosis of pulmonary tuberculosis was made, and A.P. started on the right side on 24th November, 1948.

On admission into this institution.—General examination of the patient showed his condition to be fair.

Physical examination of the chest.—Right chest showed signs of pneumothorax with deficient breath sounds and comparatively resonant percussion note. Left chest: No abnormal breath sounds.

Other systems.—No abnormal physical findings. X-ray examination showed moderate collapse of the right lung which was adherent at the top with a broad adhesion and a patent cavity.

Fluoroscopic examination.—Revealed the adhesion to be posterior.

Sputum examination.—It was positive for A.F.B. (direct smear).

Blood examination.—(Schilling's count) :

Total neutrophil	..	60
(Stab Kernig's)	..	20
Segmented	..	40)
Eosinophil	..	6
Lymphocytes	..	30
Large monocytes	..	4

E.S.R. 28 mm. 1st hour (Westergren)

It was decided to maintain the A.P. on the right side and to do closed intrapleural pneumonolysis as a supplementary operation, which was done on 3rd August, 1949.

Details of the operation.—The 1st puncture was made in the 3rd space mid-clavicular line and thoracoscope put in, which revealed one big fleshy fold-like adhesion going posteriorly; the lung surface was bluish. No tubercles were visualized either on the surface of the adhesion or the pleura. The 2nd puncture was made in the 6th space mid-axillary line, which showed the adhesion to be fairly broad and going to

the costovertebral gutter. Partial cauterization with enucleation of the adhesion was done close to the chest wall with a very dull hot cautery. Complete cauterization of the adhesion was not possible as it was very sessile. The sites of the punctures were closed with deep stitches and the patient advised to lie on the non-operated side. Subsequent and periodic screen examination of the patient showed effusion in the pleural cavity, which was showing increase in quantity at each examination. With the increase in the amount of fluid the patient started getting some rise of temperature and dyspnoea even on resting in bed.

On 2nd September, 1949.—16 oz. of straw-coloured clear fluid were aspirated from the pleural cavity. With the aspiration of the fluid, the patient was relieved of breathlessness and temperature also came down to 99°F.

24th September.—All of a sudden the patient had hæmoptysis, which lasted for four days, following which his temperature rose up to 104°F. to 105°F., for which he was administered streptomycin $\frac{1}{2}$ gm. twice a day from 6th October, 1949. In all 20 gm. were given, with the result that his temperature again settled to 99°F.

Routine fluoroscopic examination showed increase in the amount of fluid.

19th November.—2nd aspiration was done and 36 oz. of thick pus were taken out; one lakh units of penicillin in 20 cc. normal saline were put into the pleural cavity.

22nd November.—10 cc. of P.A.S. solution were put into the pleural cavity.

29th November.—3rd aspiration was done, 16 oz. of pus were taken out and 10 cc. of P.A.S. were put into the pleural cavity.

9th December.—10 cc. of P.A.S. solution were put into the pleural cavity.

13th December.—Patient started complaining of a painful swelling in the chest which showed some increase in size on coughing.

On examination it was found to be at the site of the old puncture wound of the intrapleural pneumonolysis operation in the 3rd space mid-clavicular line. The swelling could be reduced on gentle pressure and it also revealed gurgling. It was filling again after coughing.

The superficial skin was shining, stretched, slightly injected and slightly tender. Taking into consideration the underlying empyema, a diagnosis of empyema necessitatis was made.

Screen examination showed nearly half of the pleural cavity to be full of fluid. A soft gauze pad and cotton were placed at the site of the swelling and a binder was applied. The patient was instructed to press the swelling with hand while coughing and to lie on the opposite side. Subsequent examination of the patient the next day showed the swelling to be more boggy and painful.

14th December.—Three pints of pus were aspirated from the pleural cavity and one lakh units of penicillin were put in.

21st December.—X-ray of the chest was done, which showed the whole of the right chest to be opaque with a very small amount of fluid.

24th December.—10 cc. of P.A.S. solution were put in the pleural cavity.

31st December.—Following excessive coughing, the swelling in the chest wall burst and a small amount of thin yellowish creamy pus came out. A clean dressing was applied and the patient was put in semi-recumbent posture with head and upper chest raised up.

2nd January, 1950.—Two pints of pus were aspirated and one lakh units of penicillin and 1 gm. streptomycin solution were put into the pleural cavity.

Examination of pus was negative for A.F.B. Repeated examination of the pleurocutaneous sinus showed occasional thin yellowish discharge out of it. It was decided to start ultra-violet ray therapy locally on the sinus from 12th January.

13th January.—26 oz. of thin pus were aspirated, 1 gm. streptomycin and one lakh units of penicillin were put in. In all the patient had 9 exposures to the ultra-violet rays at 4 days' interval, the last being on 6th February.

13th February.—Aspiration of empyema was again done and 6 oz. of very thin pus were aspirated.

Local examination of the pleurocutaneous sinus showed it to be apparently closed and no discharge was seen coming out for at least 7 days.

Subsequently the patient had three stages of thoracoplasty and nine ribs were resected.

Follow up of the case has revealed the sinus healed; empyema space obliterated; cavity apparently closed; and sputum negative for A.F.B. For three months the patient has had no constitutional symptoms. He is on light exercise these days.

Discussion

Of the 341 cases who had closed intrapleural pneumonolysis done in the sanatorium since 1941, this complication occurred in only one case reported above. The case under review before undergoing closed intrapleural pneumonolysis had a patent cavity and a broad adhesion, which was apparently keeping the cavity open. Sputum was positive for A.F.B., hence closed intrapleural pneumonolysis was done. Clinically it has been observed that incidence of pleural effusion and empyema is more in those cases where partial cauterization or enucleation is attempted than in cases where complete cauterization of adhesion has been done.

Occurrence of empyema necessitatis at the site of the puncture wound was due to the failure of the puncture wound tract to heal completely though superficially it was closed. The various predisposing factors which prevented the tract to heal from inside were :—

(1) Infection of the tract from within the pleural cavity due to occurrence of empyema.

(2) Excessive and troublesome cough, which interfered with the healing of the wound.

Though for the complete closure of the tract the application of deep stitches has been recommended by some, in actual practice it is difficult to stitch the intercostal muscles. Later on thoracoplasty was done in this case for positive sputum, a big cavity which could not be seen because of associated empyema, pleurocutaneous sinus and the empyema space.

My thanks are due to Dr. T. J. Joseph, Medical Superintendent, Lady Linlithgow Sanatorium, for going through the case report and allowing me to send it for publication.

CUTANEOUS AMOEBIASIS

WITH A CASE REPORT

By S M GHOSH, M.B. (Cal), F.R.C.S. (Eng.)
and

ANJALI MUKHERJI, M.B. (Cal.)

Department of Surgery, Campbell Hospital, Calcutta

Amoebic infection of the skin and subcutaneous tissues is much more common than is generally realized. Diagnosis is often missed because the possibility is not thought of. Even the finding of *Entamoeba histolytica* in the faeces may not draw the attention to the possibility of an ulcer to be of amoebic in origin, because amoebic infection is not infrequent in our country. Cutaneous amoebiasis was originally described by Nasse as far back as 1892 surrounding the discharging sinus of a liver abscess, but he was not able to see the living amoebae. Menetrier and Tourane reported a case of progressive necrosis of skin and subcutaneous tissue surrounding the incision of a liver abscess. The discharge contained active amoebae. No history of dysentery was present. Autopsy confirmed the amoebic nature of the liver abscess. Selenew described four cases of desquamative and pustular dermatitis of the head, neck and trunk in adult patients, from the discharge of which he identified adult amoebae. But there is no proof that these were specimens of *E. histolytica*. Cases of amoebic infection of skin and subcutaneous tissue following drainage of liver abscess have been occasionally reported by various authors. In 1912 Maxwell read a paper before the Royal Society of Tropical Medicine and Hygiene entitled 'Fistulous disease of buttocks: a clinical entity'. He

found *E. histolytica* in the discharge from the sinus around the anus in some cases of multiple fistula in ano and suggested that the disease was due to entrance of amoebae in tissues, possibly from an original simple fissure in ano.

In 1919 Engman and Heithaus reported a case of deep serpiginous ulcers on body, buttocks and leg. The histological section as well as the pus showed *E. histolytica*. Amoebae were present in the faeces. The same authors reported a case of cutaneous amoebiasis of the dorsal surface of the hand. The pus contained cystic forms of *E. histolytica*. The case was cured after emetine injections. But there is no evidence that amoebae in the animal host can undergo encystment outside the intestinal tract.

Runyan and Herrick in 1925 mentioned two cases of amoebiasis of abdominal and thoracic wall following caecostomy and transthoracic drainage of liver abscess respectively.

Penile ulcer of amoebic origin was described by Straub which was cured with emetine.

Perianal ulceration resembling malignant condition was described by Tixier *et al.* (1927). They drew attention to the presence in their case of colonies of amoebae deep down in the dermis away from the surface ulceration.

Van Hoof (1926) described a case of spreading ulcer round anus and buttock. Rapidly spreading ulceration of the abdominal wall following drainage of appendicular abscess or colostomy has from time to time been reported by various authors.

Cases of cutaneous amoebiasis proved by histological section have been reported by Rajam and Rangiah (1939) and Mahadevan (1945).

McConaghey (1945) reported a case of fungating mass in the perianal region of amoebic origin following infection of haemorrhoids. No biopsy was done but the case responded to emetine treatment.

Very recently Kouri *et al.* (1949) reported a case of ulcerated growth in the perianal region which was diagnosed as epithelioma and radical excision was done including block dissection of glands. Subsequent biopsy proved the amoebic nature of the growth. Cutaneous amoebiasis is mainly of the ulcerative type but an allergic type of dermatitis is also described.

Ulcerative type of cutaneous amoebiasis.—It is classified into four different groups :

(a) Following drainage of amoebic hepatic abscess.

(b) Following drainage of ruptured appendix and colostomy.

(c) Cases not directly concerned with viscera.

(d) Perianal amoebiasis.

The first and the second group comprise the bulk of the literature. Various types have been described extending from a small area of ulcer

round about a discharging sinus of amœbic hepatic abscess to an extensive gangrenous condition spreading over the whole of the abdominal wall following colostomy.

The third group is rare and only one case could be traced in literature where a progressive swelling and ulceration of the abdominal wall is described, which developed after a bruise with a dirty shovel in a 48-year-old labourer with a history of recurring attacks of dysentery for 20 years. The patient came for treatment after 2 years. Biopsy revealed necrotic tissue with numerous amœbæ in the viable tissues. Stool examination showed presence of *E. histolytica*. The wound healed up with emetine injections and zinc peroxide dressing.

The fourth group, to which the case under discussion belongs, is of special importance to the surgeon because of the difficulty in diagnosis. Usually two types of lesion are seen: (i) Gangrenous type with extensive destruction of skin and subcutaneous tissue. (ii) Granulomatous type with the production of a lesion raised above the skin and resembling epidermoid carcinoma.

The cutaneous lesion is always secondary to amœbic infection of the intestine. The intestinal infection may be with or without any clinical manifestation.

The amœbæ cannot penetrate normal skin with intact cornified epithelium. In almost all cases mentioned in literature in which there is reliable verification of the diagnosis by biopsy all have had cutaneous lesions around the anal orifice following fistula in ano, fissure, etc., or from sinus leading from a liver abscess or any other abdominal focus of amœbic infection.

As to the methods of penetration of *E. histolytica* into the tissues there are two views: (1) Penetration is effected by the mechanical action of the blade-like pseudopodia extruded by the amœbæ forcing their way between the cells in their path. (2) Parasite acts directly on the tissues by means of a proteolytic secretion which dissolves the cells with which the organism comes into contact. This view is accepted by most workers.

The rôle of bacterial infection in production of ulcer is of secondary importance, though it plays an important rôle in sloughing and gangrenous changes.

Allergic type of dermatitis.—This type of skin lesion to which the term amœbides has been given, is characterized by obstinate urticaria, pruritus, and may be associated with recurrence of dysentery. It differs from the other type in that amœbæ have never been demonstrated in the skin lesion. In a considerable proportion of cases amœbæ can be demonstrated in stool and diagnosis is confirmed by their curability with emetine.

A case of cutaneous amœbic infection closely resembling an epidermoid carcinoma came under our care recently and is given below:

Case report

Complaint.—B. P., an Indian male, aged 42 years, was admitted to the Campbell Hospital on 10th October, 1949, complaining of a painful ulcerative growth accompanied with pruritus round the anal orifice of about 2 months' duration.



Fig. 1.—Perianal cutaneous amœbiasis

History.—The condition started with pain and difficulty during and after defæcation. It was quickly followed by the ulcerative condition round the anus. The pain and pruritus were of such severe degree that it interfered with his sleep and he was in constant agony.

Present condition.—An ulcerative growth (figure 1) all round extending for about 3 cm. from the margin of anus with irregular and everted margins is seen. The floor of the ulcer shows polypoid masses covered with slough here and there. The growth extends for about a centimetre into the anus involving the anal mucosa and sub-mucosa. The surrounding area is markedly indurated. Proctoscopic examination is not possible due to pain.

Inguinal lymph nodes are enlarged and tender on both sides.

The general condition of the patient is good. Much significance was not attached to the previous history of alternate diarrhoea and constipation as it is a very frequent condition in our country. From every standpoint, history, clinical course and physical findings, the condition was highly suggestive of a malignant growth.

Blood picture.—Hb: 80 per cent, R.B.C.: 45 million per c.mm., W.B.C.: 10,000 million per c.mm., poly 72 per cent, lympho 22 per cent, eosino 4 per cent and mono 2 per cent.

W.R.—Negative.

Stool.—Routine stool examination did not reveal any ova or protozoa.

Biopsy report.—Ingrowths of papillary processes in places with suggestion of cell nest formation. The picture suggests the possibility of squamous celled carcinoma.

As the clinical and histopathological examination suggested squamous celled carcinoma from the anal margin, it was decided to excise the growth after a preliminary inguinal colostomy.

On 12th October, 1949, a left inguinal loop colostomy was performed under nitrous oxide and oxygen.

In a few days after the colostomy it was found that the lesion around the anus showed signs of rapid retrogression. In about three weeks' time the growth completely disappeared. This caused a doubt about the original diagnosis. Rectal examination at that time revealed a fissure with a dorsal fistula which was excised on 11th November.

Shortly afterwards a granulomatous growth similar to the growth in the anal region appeared on the abdominal wall around the proximal opening of the colostomy extending for about four centimetres (figure 2). There was no ulceration in the mucous membrane of the gut.

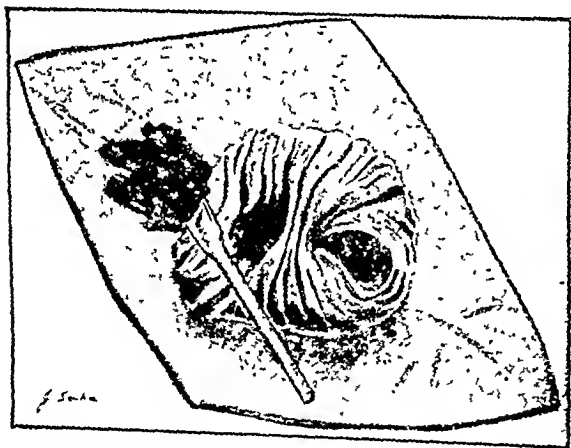


Fig. 2.—Amoebic granuloma around the colostomy opening.

Biopsy report.—Biopsy of the granulomatous tissue showed hyperplasia of the stratified epithelium, areas of ulceration and presence of chronic inflammatory changes in the sub-epithelial layer. No sign of malignancy could be seen (figure 3, plate XLIII).

On special staining a large number of *E. histolytica* was found in the ulcer (figure 4, plate XLIII).

Sigmoidoscopic examination of both the proximal and the distal loops did not show any abnormality except presence of mucus in places. Examination of the mucus and scraping from the granuloma revealed vegetative form of *E. histolytica*.

Treatment with emetine injection and chiniofon wash was at once instituted. After four injec-

tions of emetine the granuloma disappeared completely.

On 19th December, 1949, an extraperitoneal closure of the colostomy was done under nitrous oxide and oxygen anaesthesia. Patient had an uneventful recovery and was discharged on 14th January, 1950.

Discussion

The presence of *E. histolytica* in the tissues and the dramatic response to emetine leave no doubt about the amoebic nature of the lesion, diagnosis of which was missed in the beginning as the possibility was not thought of. The history of attacks of alternate diarrhoea and constipation which is a common feature in amoebiasis was ignored in view of the fact that the site, progress of the lesion, clinical history and physical findings were such as would justify the diagnosis of carcinoma. The suggestion of cell nest formation in the biopsy report appeared to confirm the clinical diagnosis. On reviewing the histological report on the basis of subsequent events, one is reminded of the suggestion of Boyd that any chronic infection prevents the epithelium from covering the raw surface and it may send long processes down into cutis vera giving a picture which may closely resemble an early carcinoma.

As to the pathogenesis of the lesion in this case, possibly the fissure in ano served as the portal of entry of *E. histolytica* into the surrounding skin. Craig points out in his treatise on amoebiasis and amoebic dysentery that 10 per cent of hospital cases in India examined for *E. histolytica* were positive for the parasite. Despite such a common incidence of the infection and the well-established fact of the parasite being tissue invader it is surprising that so few cases are reported in literature.

In the perianal region most of the cases described were of spreading gangrenous type. In reviewing the literature we have seen few cases resembling the case under discussion.

Summary

1. The note of a case of cutaneous amoebiasis affecting the perianal region and abdominal wall close to a colostomy wound is presented. Perianal growth closely resembled carcinoma. *E. histolytica* was found in the tissues in biopsy material and in mucus collected by sigmoidoscopy. The ulcers rapidly healed after emetine therapy.

2. In any ulcerative or granulomatous lesion of the perianal region the possibility of amoebic infection should be kept in mind. But it must be remembered that the condition is very rare. In fact when such findings justify the diagnosis of malignancy every attempt should be made to exclude the possibility of malignancy before a conservative line of treatment is adopted.

3. The literature on the subject is reviewed.

We are grateful to Dr. A. K. Dutta Gupta, Principal and Superintendent of the Campbell Medical College Hospitals for kindly allowing us to utilize the case records, to Mr. P. Chatterji, Professor of Surgery, Medical College, Calcutta, for his valuable suggestions, and to Dr. P. C. Sen Gupta, Officer in charge, Kala-azar Research Department, School of Tropical Medicine, Calcutta, for kindly doing the special staining for *E. histolytica*.

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THE RELATIONSHIP OF THE BODY- WEIGHT TO THE WEIGHTS OF THE ORGANS

THE BRAIN

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and

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In continuation of our paper (1949) on the studies of the weight of the heart we present below data in relation to the weight of the brain of normal adults.

A carefully selected group of 46 cases forms the subject of this short note. Selection was based on elimination of cases, where the brain was likely to have been affected by trauma, and pathological processes. The age group has again been between 18 years and 30 years. Only those cases which did not show significant alteration in body-weight by cold storage were included. In this group of 46 cases there were 5 females and 41 males.

As the total number of female bodies in the series is only 5, no significant statistical data can be deduced and hence the actual brain-weight and ratio of brain-weight to body-weight for all 5 cases are set out in table I without any statistical conclusions.

TABLE I
Females (5)

Age	Body-weight in Kg.	Ratio of brain to body-weight	Brain-weight Gm.
20	37.02	30.6957	1,160
20	40.25	34.69	1,360
22	39.04	24.0152	1,360
22	55.50	50.454	1,100
24	39.04	34.3502	1,030

In the case of male bodies, the results are shown in table II. It was possible to study these in more details and an attempt is made in this note to arrive at statistically significant figures for the subjects under study.

The range of the brain-weight varied from 1,020 gm. to 1,470 gm., the variation being independent of the body-weight. The mean brain-weight in this age group of adult males was 1,218.72 gm. with a standard deviation of 84.824 and a coefficient of variation 6.76. This should give an approximate idea of normal adult brain-weight in Indian male subject.

The weight of the brain was taken after wiping it superficially with a sponge and after removal of the dura mater. The brain, cerebellum, pons and medulla were weighed together.

Jones (1946) gives the normal brain-weights as 1,360 gm. in males and 1,250 gm. in females. These are higher than our male series. Gray (Johnston and Whillis, 1946) states that in the series of 278 males, the maximum brain-weight was 1,840 gm., the minimum brain-weight was 964 gm., and the average brain-weight was 1,380 gm. In the series of 191 females, the same author obtained a maximum brain-weight of 1,585 gm., a minimum brain-weight of 879 gm., and an average brain-weight of 1,250 gm. The age group and statistical mean, S.D. and variation coefficient are not stated. Cunningham (Brash and Jamieson, 1943) gives the average adult brain-weight in males as 1,350 gm. and of females 'rather less'.



Fig. 3.—Microphotograph (low power) showing down growths of epithelium and chronic inflammatory changes in the dermis.

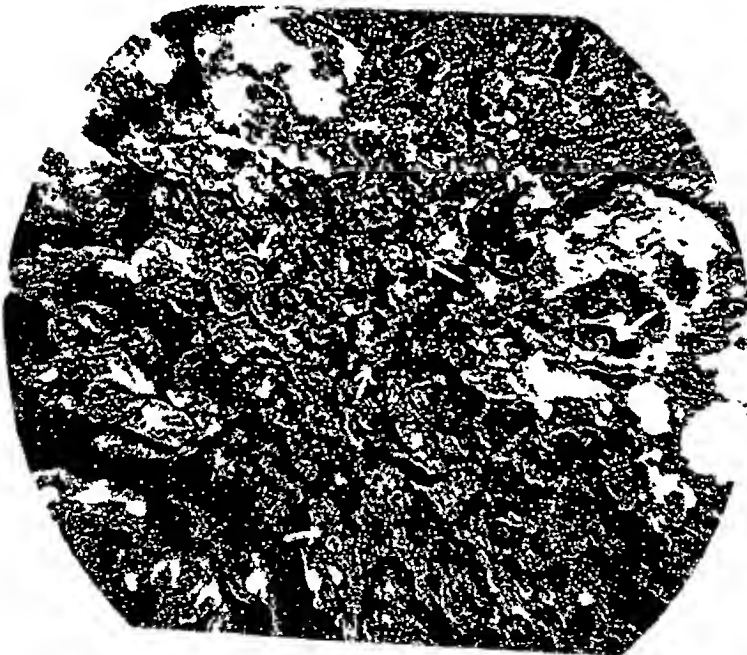


Fig. 4.—Showing numerous *E. histolytica*. Those showing the typical nucleoli are marked with arrows.

TABLE II
 Males (41)

Age	Body-weight in Kg.	Ratio of brain to body-weight	Brain-weight Gm.
18	41.76	31.570	1,250
18	69.60	45.360	1,450
18	45.60	35.1025	1,200
18	39.36	29.7501	1,250
20	51.78	37.932	1,290
20	47.04	33.6759	1,320
20	38.40	28.2500	1,270
20	49.32	32.4222	1,350
20	58.56	41.923	1,320
20	40.00	41.802	1,471
20	55.48	35.794	1,020
20	45.12	32.2685	1,230
20	55.68	36.7197	1,260
20	42.72	32.575	1,240
23	49.44	42.6259	1,150
23	51.60	35.5924	1,370
25	56.16	37.908	1,400
25	56.64	41.8157	1,280
25	40.00	32.0585	1,330
25	59.04	41.3277	1,350
25	49.92	36.8542	1,280
25	44.40	38.6755	1,240
25	41.00	33.064	1,350
26	50.88	36.5824	1,250
28	50.88	38.4355	1,260
28	50.88	39.1947	1,250
28	48.00	36.288	1,250
28	53.76	37.0805	1,370
28	37.44	24.0152	1,250
30	45.27	36.879	1,250
30	53.76	36.288	1,400
30	51.12	37.7405	1,280
30	47.60	47.4468	1,140
30	44.76	34.0707	1,240
30	58.08	37.3371	1,470
30	55.48	42.0940	1,250
30	50.88	40.1509	1,230
30	48.48	37.2463	1,230
30	56.64	43.1651	1,240
30	48.48	31.4675	1,440
30	40.00	31.3517	1,360

These authors feel that 'difference is simply related to smaller weight of the body in females. If body-weight is discounted, it appears that the difference in relative weights in the two sexes is insignificant'.

Both these European authors met with higher weights than those in our series. No authentic Indian figures are available so far. Mody (1947) gives average brain-weight of 47.34 oz. (1,420.2 gm.), the minimum brain-weight of 35 oz. (1,050 gm.), and a maximum brain-weight of 57 oz. (1,710 gm.), for males. The same author gives the average brain-weight of 38.29 oz. (1,151.7 gm.), the minimum brain-weight as 30 oz. (900 gm.), and a maximum brain-weight as 48 oz. (1,240 gm.), for females. In our previous paper (1949) on heart-weights we have pointed out difficulties in accepting these figures as representative for the Indian population.

Brain is an organ which increases rapidly in weight in the first year of life and grows speedily till the age of six years, when it makes up 85 per cent of adult weight. The increase

in bulk is due to myelination of tracts. This increase has to run *pari passu* with the size of the cranial cavity. It is so situated that it fills up this closed box completely. As yet, we have no means to assess the relation of brain-weight to intellectual function. Cunningham (Brash and Jamieson, 1943) remarks that though variations in weights met with are considerable, it is extremely unlikely that normal intellectual functions can be carried out by brain weighing less than 1,000 gm. We had no opportunity to assess intellectual functions in our series and none of the brains of our cases weighed so little, nor was any case recorded as mentally defective. In general the powers of memorizing are said to be better developed in Indians but perhaps this does not necessitate so much increase of weight as increase of gyri and sulci to give increased cortical area. In old age the brain-weight diminishes very slowly but Gray (Johnston and Whillis, 1946) states that in any case it is not reduced by more than 28 gm. in all.

Turning to another aspects of consideration and one to which Cunningham has made a passing remark, we have compared ratios of brain-weights to body-weights to do away with vagaries arising out of significant differences in body-weights. The ranges of such ratios are 24.0152 to 47.4468 and the mean of ratios is 36.678 with S.D. of 4.628 and coefficient of variation of 12.45. Only such ratios could be compared with population of other countries. We have not come across similar published records from elsewhere.

We take this opportunity to once again remark that these figures are only a result of planned study of a limited group of males from autopsies in Bombay over a fairly long period and cannot necessarily be representative of a cross section of the population.

Summary

Brain-weights, body-weights, and ratios of brain-weight to body-weight are presented with statistical mean, C.D. and S.D. for brain-weight and the ratios for males of age group 18 to 30 years.

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[The statistical analysis may be subject to revision.—
 EDITOR, I.M.G.]

EPIDEMIC DROPSY

A NEW TEST FOR ARGEMONE OIL

By R. N. CHAKRAVARTI

R. N. CHAUDHURI

and

N. K. CHAKRAVARTY

(From the Epidemic Dropsy Enquiry, Indian Council of Medical Research, School of Tropical Medicine, Calcutta)

Introduction

EPIDEMIC dropsy is a disease occurring in epidemic or endemic form characterized clinically by oedema, erythema, cutaneous nodules, diarrhoea, cardiac failure, glaucoma and/or abortion in pregnant women. Pathologically there is an extensive dilatation and engorgement of the capillaries in the skin and the internal organs. Its aetiology has been traced to the use of adulterated mustard oil, the chief cooking fat of a large section of the Indian population. Subsequent work has shown that the disease is primarily a toxic condition produced by the adulterant argemone oil which is extracted from the seeds of the plant *Argemone mexicana* that grows wild.

The toxic properties of argemone oil were, however, known as long ago as 1878 when accidental poisoning from the use of this oil in food was reported in a number of cases (Lyon, 1889). Apparently this fact has been overlooked by the recent workers in this field.

Detection of toxic oil

The detection of argemone oil in mustard oil is, therefore, an essential step for the supply of pure oil and for the maintenance of the health of the community. The problem engaged the attention of some workers in the past, and three *chemical tests* have been in use for the purpose, viz: (1) nitric acid test,* (2) cupric acetate test (Lal *et al.*, 1939) and (3) ferric chloride test (Sarkar, 1941; Sen, 1946). The *physical tests*, such as spectrophotometric and fluorescence tests, are of indefinite value and have little practical utility and no simple *biological test* on laboratory animals has yet been developed (Lal *et al.*, 1939, 1941a). The *feeding experiments* on human volunteers with the toxic oil proved successful (Lal *et al.*, 1937, 1941b; Chopra *et al.*, 1939) but it can have no place as a test measure.

Of the three chemical tests mentioned above the nitric acid test is very simple but non-specific,

*There is some doubt regarding the originator of the nitric acid test. Lal *et al.* described the test in 1939 and Sarkar (1941) referred to it as the 'test of Lewkowitsch and Warburton' (1922), although in the reference quoted by him it is mentioned under *A. speciosa* and not *A. mexicana*. A detailed description of the test can, however, be traced as far back as 1888 (Lyon, 1889).

yielding positive results with many other oils, viz, linseed oil, *mahua* oil, niger seed oil, safflower seed oil, sesame oil, olive oil, jute seed oil, tamarind oil and radish oil (Sarkar, 1942). The cupric acetate test also has not yielded consistent and reliable results. The ferric chloride test is specific and in its modified form detects argemone oil in a concentration of 0.25 per cent. But the procedure for this test is rather complicated and a microscopic examination may be needed when the oil is present in minute amounts—a positive reaction being indicated by the appearance of a reddish-brown acicular precipitate in small lumps which tend to adhere to the acid (hydrochloric acid used for the test)-oil interface. Another drawback of the test is that it cannot be developed properly for the colorimetric estimation of argemone oil because of the presence of the coloured ferric ion in the acid layer. The quantitative method developed from the colour in the acid layer of the nitric acid test (Lal *et al.*, 1940) is unreliable since other oils used as adulterants might account for part or whole of the colour, and this may wrongly be attributed to argemone oil. Sarkar and Rahaman (1945) described a quantitative method but besides the fact that it involves a complicated procedure, it is only capable of estimating argemone oil in a concentration of 5 per cent or more.

We, therefore, undertook to develop a test for argemone oil that should be simple, sensitive and practicable in the least equipped laboratory. The present test satisfies these conditions; it also needs only a small amount of the suspected oil and depends on a colour reaction which may be utilized for quantitative colorimetric estimation. The test is described below:—

The test

Reagent.—Two volumes of concentrated hydrochloric acid (S.G. 1150 to 1155) diluted with one volume of distilled water (i.e. about 20 per cent HCl w/w).

Procedure.—Part of the sample of suspected mustard oil is filtered. 2 cc. of the filtered oil are mixed by gentle shaking with an equal volume of ether in a $\frac{1}{2}$ inch \times 4 inches test tube and 0.3 cc. of the above reagent is added. The test tube is then well plugged with cotton-wool and kept for 16 hours. An orange colour of the lower acid layer at the end of this period indicates the presence of argemone oil in the original sample.

The colour can be discharged by the addition of a few drops of concentrated sodium hydroxide solution or liquor ammonia and can be made to reappear by the addition of a few drops of concentrated hydrochloric acid. The colour can also be discharged by the addition of a small piece of zinc. In cases where the adulteration is fairly high, orange needle-shaped crystals have

been found to separate out at the acid-oil interface.

Comment

This test is extremely sensitive, being found positive in a concentration as low as 0.1 per cent and is at the same time extremely simple. It does not require elaborate laboratory facilities and very little manipulative skill is necessary. It can be carried out with the minimum of labour and attention. The dilution with ether is not essential but appears to help the development of the colour.

We have outlined here the result of our preliminary work on the new test for argemone oil and further investigation is in progress along the following lines :—

1. The effect of time, temperature and other reagents to develop the test.
2. The effect of other aqueous acids in place of hydrochloric acid.
3. The development of the test for the colorimetric estimation of argemone oil in mustard oil.
4. The effect of adulteration with various other oils on the test.

The results on these lines will shortly be communicated in detail for publication.

Our grateful thanks are due to Lt.-Col. S. D. S. Greval, I.M.S. (R.), for kindly drawing our attention to the reference on argemone oil poisoning in Lyon's *Textbook of Medical Jurisprudence for India*, a new edition of which he is preparing.

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CORRIGENDA

In the article on 'Treatment of Epidemic Dropsy' by R. N. Chaudhuri and N. K. Chakravarty in April 1950 issue of this journal—

- (1) Page 165, 2nd column, lines 10-15 : in place of 'Bailey Robinson and Staunton.....7:8:4:5'-tetramethoxy-3:4 dihydro-1:2 benzphenanthridone' read as follows—'Sanguinarine and dihydro-sanguinarine have not yet been synthesized but one of their degradation products, N-methyl-7:8:4:5'-tetramethoxy-9:10-dihydro-1:2-benzphenanthridine, retaining the full skeleton of sanguinarine, has lately been synthesized by Bailey, Robinson and Staunton (1950).'
- (2) 'Sanguinerine' should be read as 'Sanguinarine'.
- (3) Page 172, Reference No. 6—in place of 'Chopra, R. N., Chaudhuri, R. N., and De, M. N.', read 'Chopra, R. N., Chaudhuri, R. N., and De, N. N.'
- (4) Page 170, col. 1, line 9 : in place of 'sclerotomy' read 'sclerectomy'.

A Mirror of Hospital Practice

A CASE OF SUBMUCOUS FIBROID SIMULATING PREGNANCY

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Midwifery and Gynaecology, National Medical
Institution, Calcutta

Mrs. U. B., aged 24 years, para 4, last child 8 years before, all the children are living, all

deliveries were normal, no history of any abortion.

Suddenly I was called in at about 8 p.m. on 7th December, 1945.

Complaints.—(1) Bleeding per vaginum, slight for the last few days, increased since morning and profuse since evening.

(2) Pain in the lower abdomen, slight for about 15 days, increased since morning.

(3) Amenorrhœa—6 months.

The patient was moderately built and anæmic. A hard mass in the lower abdomen up to the level of umbilicus. No foetal heart sounds were heard. No foetal parts were palpable.

Menses.—Previously regular and lasted for 4 or 5 days. For the last 4 to 5 years regular but lasting 7 to 8 days, the bleeding more than before.

Last menses.—In the early part of Ashar, i.e. in the third week of June.

There was no history of vomiting, œdema of legs or scanty urine either during this or previous pregnancy. No history of fall or any other injury.

P.V.—External os, 1 finger tight.

Treatment.—Morphine gr. $\frac{1}{4}$, atropin gr. 1/100 injected; glucose 25 per cent 50 cc. intravenous injection.

Bleeding diminished, and within an hour the patient fell asleep.

On 8-12-45.—There was neither any bleeding nor any pain. A sedative mixture of chloral hydrate gr. xx and pot. bromide gr. xx b.d. and kapillin 10 mg. b.d. were advised. Cal. gluconate 10 per cent 5 cc. with redoxon 100 mg. intravenous injection daily was also advised.

No foetal heart sounds were heard, no foetal parts were palpable. The feel of the uterus was harder than that of pregnant uterus. B.P. 105/75. Therefore, x-ray of the uterus was advised.

On 9-12-45.—At about 9 p.m. there was profuse bleeding per vaginum and the patient was feeling severe pain in the lower abdomen. The height of fundus was the same as before, uterine contraction was good. Morphine gr. $\frac{1}{4}$ injected.

Glucose 25 per cent 50 cc. intravenous injection. Then normal saline 1 pint with 100 cc. of 25 per cent glucose intravenously very slowly injected. Hæmorrhage diminished. The patient did not sleep.

One dose of chloral hydrate and bromide mixture was given. The patient fell asleep within an hour. Bleeding stopped.

On 10-12-45.—After a few hours the patient awoke complaining of pain in the lower abdomen with slight bleeding per vaginum.

P.V.—External os, 2 fingers loose. A mass harder than placenta and not adherent in the lower portion of the uterus was felt.

The bleeding increased.

Glucose 25 per cent 50 cc. intravenously injection. Pain in the lower abdomen increased.

Another dose of chloral hydrate and bromide mixture administered and morphine gr. 1/6 injected. Pain and hæmorrhage per vaginum diminished.

In the morning at about 6 a.m. a globular mass, size of a foetal head, came out with profuse bleeding. After that the hard mass in the lower abdomen diminished in size and was felt just above the symphysis pubis.

P.V.—Cervix dilated and nothing was felt in it.

Ergometrin 1 cc. was injected. Bleeding diminished. The patient fell asleep, after that recovery was uneventful.

The oval mass, spontaneously delivered, measured $3\frac{1}{2}$ inches by 3 inches. Cut section revealed the whirled appearance characteristic of fibromyoma with somewhat hæmorrhagic margins. Section revealed interlacing bundles of smooth muscle and fibroblastic cells.

Diagnosis.—Fibromyoma.

A few days later, when asked, the patient stated that she felt a mass in her lower abdomen just above the symphysis pubis for the last few months which was gradually increasing without any complaint. She had a slight morning sickness during her first pregnancy only, not in the second, third and fourth.

She was treated for anæmia with iron, liver extract and marmite, etc., and improved rapidly. Within 5 or 6 months she menstruated, since then the menstruation was regular and normal till December 1947. Since January 1948 she had no menstruation. She had become pregnant. The pregnancy was normal. She was delivered of a healthy male baby on 17th September, 1948, without any difficulty. There was no post-partum hæmorrhage. Puerperium was normal.

Comment.—In submucous fibroid menorrhagia and metrorrhagia are the common symptoms. But this patient had amenorrhœa for 6 to 7 months. Probably it was due to anæmia, the growth of fibroid is generally slow but in this case the growth of fibroid was rapid because the patient noticed the tumour just above symphysis pubis 6 to 7 months before. Within 6 to 7 months it reached the level of umbilicus. Due to amenorrhœa and centrally situated mass in the lower abdomen the patient thought that she was pregnant. She had no morning sickness in her previous pregnancies excepting the first one. Then there was pain in the lower abdomen with contraction of uterus simulating labour pain. Was it due to the irritation by the tumour which acted as a foreign body when it was detached partially from the uterine cavity?

Due to contraction of the uterus the cervix dilated and the tumour was delivered like foetus without any external aid. Over and above that the patient was a multipara with 4 healthy children before without any abortion. Again 2 years after the expulsion of the tumour she became pregnant and was delivered normally of another healthy baby.

Indian Medical Gazette

AUGUST

LEPROSY TAMED

Hope was brought to the leper by Sir Leonard Rogers in Calcutta in 1915 (Megaw, 1950). His new preparations from old remedies reduced the period of treatment considerably. In one year he cured a brother officer who remained free from relapse for ten years (until killed in an accident). His work, on his retirement from the I.M.S. in 1926, was taken up by Dr. E. Muir who made to the treatment a few additions, including an intensive treatment with the original chaulmoogra oil. Dr. Muir, in the Calcutta School of Tropical Medicine, was followed by Dr. John Lowe and the latter by Dr. Dharmendra, the present head of the department of leprosy in the School.

The next advance in treatment came in 1943 from the U.S. National Leprosarium, Carville (Faget *et al.*, 1943). The sulphone drugs had been introduced. Typically, in the aromatic series, they consist of two benzene rings linked by one molecule of sulphur dioxide. In 1947, Dr. Muir in a report from the West Indies said that for the infective type of leprosy he had not seen any drug so successful as the sulphones (Muir, 1947).

In 1950 appeared an account of the treatment in Nigeria by Dr. Lowe (Lowe, 1950; abstract in this journal, Current Topics, 1950).

In this issue Dr. Dharmendra has written at length on the present status of sulphone treatment in leprosy (p. 348). A lengthy abstract of another paper appears on p. 370.

From the start made by Sir Leonard Rogers in Calcutta in 1915, with salts made from a well-known oil to the introduction of the sulphones in 1943, in 26 years, leprosy has been tamed.

The cost of taming suits the alleged Asian poverty. The annual cost of treating a leper need not exceed Rs. 30, following a bi-weekly injection method of treatment as practised in Calcutta at the School of Tropical Medicine and the Gobra Leprosy Hospital (Sen, 1950).

Incidentally, the early sulphones were at first considered unsuitable. We should not be surprised if streptomycin, specially along with PAS, is found to succeed also, on further trial. It has been so far considered unsuitable.

The taming was preceded by a loss of prestige: Nerve leprosy was no longer considered infectious. The patients were no longer segregated. Another possibility suggests itself: Is *Mycobacterium lepræ* like its cousin *Mycobacterium tuberculosis hominis* a dying organism? It is well known that a decline in tuberculosis was recorded in England long before any measures were taken against it (Wilson and Miles, 1946).

Something similar appears to have occurred to leprosy also: it has disappeared from wide geographical tracts steadily since the middle ages. Its course also appears to have become mild. Its terror as given in the Old Testament, the practice of throwing handfuls of earth and performing a burial service on the newly isolated lepers in Europe in the middle ages (Rogers, 1950) and burying alive of lepers in India (Greval, in press), all point to the same conclusion. Thinking obviously retrospectively from the present position, some writers have stated that the infectivity and gravity of leprosy have been seriously over-estimated (Hyman, 1946). The Indian opinion is that all types of leprosy have always been milder here than elsewhere.

Among the many remedies for this ancient disease has been included a multitude of preparations from minerals, vegetables and animals. One such fairly recent preparation is diphtheria toxoid which has proved efficacious in Thailand (Siam) but not in the U.S.A. (Hyman, *loc. cit.*). Its synergic aid may be useful. The fact that in the immunization against diphtheria the toxoid (APT) can be given more safely to young children than to older children and adults (Parish, 1948) suggests that an allergic state in the subjects is responsible for a reaction. The reaction due to one allergic state, namely, sensitization with diphtheria, may help against another allergic state, namely, sensitization with leprosy. It is an observed fact that in cases of multiple sensitivity desensitization with one of the antigens concerned renders the subject non-sensitive to other antigens also. The first reaction forms in the sensitive cells a pattern which prevents further antigen-antibody reactions. It is possible to evoke with the toxoid intentionally a mild desensitizing reaction.

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Special Article

THE PRESENT STATUS OF SULPHONES IN THE TREATMENT OF LEPROSY

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TILL recently the only effective remedy against leprosy was the age-long treatment with hydnocarpus oil. In the early years of the present century, this treatment had undergone a great improvement inasmuch as the oil and its preparations are now given parenterally in place of the oral administration of the oil. The treatment with injections of hydnocarpus oil and its derivatives has its advantages, but has serious limitations. During the last decade, a great advance has been made in the treatment with the introduction of the sulphone drugs which are allied to, though different from, the sulphonamide drugs.

The use of sulphones was first started in the National Leprosarium in the United States of America in 1941, and the first report of this trial was published in 1943. Since then these drugs have been widely used, and the results indicate that the introduction of sulphones has marked a great advance in the treatment of leprosy, specially of the more serious type.

During the last 7 years, investigations on the subject have been increasing, and the work has been well summarized by Faget (1947) and Sharp and Payne (1948). In the present article it is proposed to survey the present status of these drugs in the treatment of leprosy.

Historical

Fromm and Wittmann (1908) first prepared diamino-diphenyl-sulphone during their researches in dye chemistry. This compound did not receive any attention till 1937 when Buttle *et al.* (1937), Fourneau *et al.* (1937) and Bauer and Rosenthal (1938) found that this substance had a great anti-bacterial power against streptococcal infection in mice and to some extent in rabbits and monkeys. Buttle *et al.* (1937) found that in man a single dose of 300 mg.

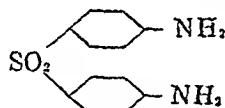
THE SULPHONE DRUGS USED IN LEPROSY

CHEMICAL COMPOSITION

FORMULA

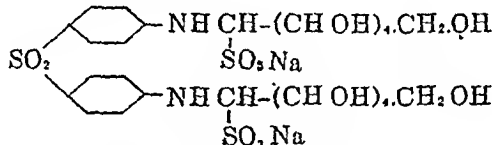
PROPRIETARY NAME AND MANUFACTURER

4,4'-diamino-diphenyl-sulphone
(The parent compound of the group)



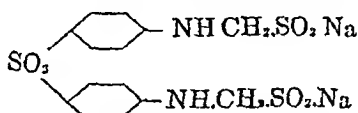
AVLOSULPHONE
Imperial Chemical Industries Ltd.
DIPHONE
Bengal Immunity Co., Ltd.

p:p'-diamino-diphenyl-sulphone-N,N'-
di-dextrose sodium sulphonate.



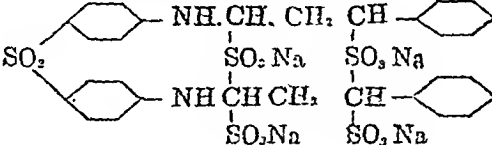
PROMIN
Parke, Davis & Co.

Disodium-formaldehyde-sulfoxylate
diamino-diphenyl-sulphone.



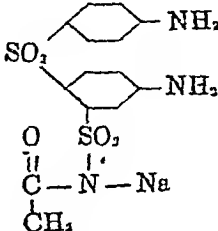
DIASONE
Abbott Laboratories
DIAMIDIN
Parke, Davis & Co.

Tetracosdiumphenyl-propylamino-
diphenyl-sulphone.



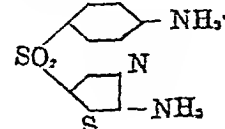
SULPHETRONE -
Burroughs Wellcome & Co.
NOVOTRONE
Bengal Chemical & Pharmaceutical
Works Ltd.

Sodium 4,4'-diamino-diphenyl-sulphone
2-acetyl sulphonamide.



PROMACETIN
Parke, Davis & Co.

2:4-diamino-5-thiazolylphenyl
sulphone.



PROMIZOLE
Parke, Davis & Co.

produced definite anti-bacterial effect in the blood. Later (quoted by Lowe, 1950) the drug was tried in human beings with acute infections, in doses of 1 to 2 gm. a day, but the treatment was soon abandoned because of the rapid production of met-haemoglobinemia and other toxic effects. The drug was, therefore, not used for treatment of infection in man, though it has established itself as a powerful anti-bacterial agent in veterinary medicine. The interest in the drug was revived when Rist *et al.* (1940) showed its favourable effects in experimental tuberculosis in rabbits and guinea-pigs.

Because of the toxic effects of the diamino-diphenyl-sulphone various attempts have been made to produce a derivative which would be safe and effective. The first derivative was made in 1937 under the name of promin; later other derivatives such as promizole, diasone, sulphetrone and promacetin have been produced.

The findings of Rist *et al.* (1940) and Feldman, Hinshaw and Moses (1940) regarding anti-tuberculous activity of the sulphones was followed by extensive trials of the parent compound and its derivatives in experimental tuberculosis in guinea-pigs, and of the derivatives in human tuberculosis. In this connection the work of Feldman and his associates stands out prominently; and information on the subject has been well summarized by Feldman (1946). The drug was found to be very effective in experimental tuberculosis but the findings in human tuberculosis have not been consistent, with the result that the drugs have not been generally adopted in the treatment of tuberculosis.

Although the sulphone drugs have not proved very useful in the treatment of tuberculosis, they have given very encouraging results in leprosy. Promin was the first sulphone drug to be used in the treatment of leprosy, and treatment with this was started in the National Leprosarium in 1941. Later, other members of the group have been used at this Leprosarium and at other leprosy centres. All the workers who have used these drugs in the treatment of leprosy have without any exception reported favourable results.

The Sulphones Used in Leprosy

As stated earlier, the demonstration of the high anti-bacterial powers of the diamino-diphenyl-sulphone (DDS)*, together with the fact that it was too toxic for human use, was followed by a search for a relatively non-toxic but equally effective derivative. This search resulted in the production of a number of compounds, most of which are simple derivatives

of the parent compound with various side chains added to the amino radicals.

The derivatives of DDS that have been used in the treatment of leprosy are promin, diasone, promizole, sulphetrone and promacetin. Of these promizole and promacetin have so far been used on only a limited scale, while the other three (promin, diasone and sulphetrone) have been widely used. The parent compound itself has of late been used in very small doses. The chemical structure of these preparations is given in the accompanying table. Detailed information about the individual drugs is given in the following account.

Promin

General.—It is the sodium salt of diamino-diphenyl-sulphone (di-dextrose sodium sulphionate diamino-diphenyl-sulphone). It is highly soluble in water and is usually used as a 40 per cent watery solution.

Reports of use in leprosy.—This was the first sulphone drug to be used in the treatment of leprosy. Faget *et al.* (1943) made a preliminary report on its successful use at the National Leprosarium, Carville, since 1941. They found the drug highly toxic when given by mouth and therefore used it intravenously. Later, Faget (1945) and Faget *et al.* (1946) made a fuller report on the treatment and concluded that the drug had a specific action on the disease. Mom (1946), Wharton (1946), Da Costa and Diniz (1946), Fiol *et al.* (1948), Dharmendra and Chatterjee (1947), Dharmendra (1948), and Floch and Camain (1948) reported on beneficial results of promin treatment from countries outside the United States of America, all using the intravenous route as suggested by the Carville workers. Cochrane *et al.* (1949) reported on 'two-and-a-half-years' experiment work on the sulphone group of drugs, and said that promin was used first but was soon dropped because of its toxicity. Herrera (1948) reported on the use of promin solution intradermally into the nodules. Information on the use of promin is also found in the reviews on the sulphone drugs by Faget (1947), Faget and Erickson (1948), Johansen and Erickson (1948), and Sharp and Payne (1948).

Toxicity.—When given by mouth promin was found to be very toxic. Hinshaw and Feldman (1941) reported that a dose of 1 to 3 gm. by mouth was attended with toxic symptoms. Faget *et al.* (1943) found the drug highly toxic when given by mouth in 0.5 to 1 gm. doses, whereas much higher doses could be tolerated by the intravenous route. Promin has, therefore, been used by the intravenous route. In common with other sulphone drugs, it produces anaemia; other toxic symptoms include nausea, vomiting, epigastric pain and discomfort, weakness, dizziness, cyanosis, drug rash, and mental confusion.

* Following the lead of the *International Journal of Leprosy* (1949, 17, 300), 'DDS' has been adopted as the abbreviation for 4,4'-diamino-diphenyl-sulphone, the other abbreviations used by some other workers being 'D.A.D.P.S.' and 'D.A.D.S.'.

Dosage.—The average intravenous dose is from 2 to 5 gm. (5 cc. to 12.5 cc. of promin solution) administered daily for six days in a week. Higher doses have been used without any apparent advantage.

Blood concentration.—The average blood concentrations of promin after a dose of 4 to 5 gm. given intravenously are about 10 to 15 mg. per 100 cc. of blood. This concentration is reached within two hours after injection, and the drug is quickly eliminated so that practically no drug is found in the blood 24 hours after the injection. Ross (1947) reported that only traces of promin remained in the blood six to eight hours following the intravenous administration of 5 gm., but that after prolonged treatment there is some accumulation since concentrations of 0.5 to 1 mg. per cent in the blood were found after 9 days' rest period in the patients who had taken the drug for 3 to 6 years.

Diasone

General.—Diasone is disodium-formaldehyde-sulfoxylate-diamino-diphenyl-sulphone. This compound is freely soluble in water.

Reports of use in leprosy.—Muir (1944) was the first to use and report on the encouraging results obtained in the treatment of leprosy with diasone, in Trinidad. Fearing that diasone like promin might be toxic by mouth he first gave it intravenously, but later he (Muir, 1946, 1947) found that it was well tolerated orally. The oral route is now the routine method of administration of the drug. Faget and Pogge (1945) and Faget (1947) next reported from the Carville Leprosarium on the beneficial effects of diasone given orally in the doses of 1 gm. daily. Fernandez and Carboni (1946), Dharmendra and Chatterjee (1947), Dharmendra (1948), Floch and Camain (1948) and Cochrane *et al.* (1949) have reported on the successful use of diasone from other centres. Information on the use of diasone is also found in the reviews on the sulphone drugs by Faget and Erickson (1948) and Sharp and Payne (1948).

Dosage.—Treatment with diasone is started with 1 tablet ($\frac{1}{3}$ gm.) daily and the dose is gradually increased to 6 tablets (2 gm.) daily according to the tolerance of the patient. In the writer's experience most patients in India do not tolerate the maximum dose well, and complain of headache, dizziness and weakness when the dose is increased above 4 tablets a day ($1\frac{1}{3}$ gm.). The Carville workers used it in the dose of 1 gm. a day.

Absorption.—After oral administration the sulphone derivatives are known to be incompletely absorbed. Smith (1949) found that diasone is incompletely absorbed from the gut, 20 to 67 per cent of the daily oral intake being recoverable from the faeces and 53 per cent being recoverable from urine. However, he found that diasone was better absorbed than

sulphetrone, and that the absorption of diasone compares with that of some of the earlier sulphonamides.

Blood concentration.—Ross (1947) reported that diasone blood levels averaged 1 mg. per cent 12 hours after the evening dose in patients taking 1 gm. daily. She found that with administration of 1 gm. diasone daily for a period of 1 to 4 years, blood concentration was maintained at levels varying from 0.0 to 3.6 mg. per cent. Dharmendra (1948) reported blood concentrations varying from 0.5 to 3 mg. per cent, on the average about 2 mg. per cent. He also reported that the blood concentration on the same dose tended to fall when the patient had been under treatment for some time without any break. Smith (1949) has found that with a daily dose of 1.2 gm. blood concentration of diasone was 1.5 mg. per cent and with a daily dose of 2.7 gm. it was 4.0 mg. per cent.

Promizole

General.—It is a compound in which an aminothiazolyl radical replaces one of the aminophenyl groups of the parent compound. It is very sparingly soluble in water (0.03 per cent), but is highly soluble in dilute acid and in some organic solvents.

Reports of use in leprosy.—Faget (1946) and Faget, Pogge and Johansen (1946) published a preliminary report and Johansen and Erickson (1947) made a further report on the use of promizole in the treatment of leprosy in the Carville Leprosarium. They reported that it was slightly less toxic than promin and diasone, but that it had no other advantage. On the other hand it is synthesized with difficulty and is therefore more expensive. The use of the drug has consequently not been extended.

Toxicity.—Promizole is considered to be relatively free from toxicity. The urine of patients receiving promizole is reported to develop a characteristic pink colour due to unidentified dye formation as a degradation product of promizole, but this has no harmful effect.

Dosage.—Daily dosage of 1 gm. is given initially in divided doses of 0.5 gm. each and increased slowly up to a daily dose of 5 gm. The manufacturers recommend that after six months of treatment at higher levels, dosage should be reduced to 1 gm. daily.

Blood concentration.—Ross (1947) found that with a daily dose of 6 to 7 gm. of promizole, the blood levels decline rapidly and reach 1 to 2 mg. per cent 12 hours after the last dose, large amounts being eliminated in the urine.

Promacetin

General.—This compound is sodium 4:4'-diamino-diphenyl-sulphone-2-acetyl sulphonamide. It is a white crystalline compound

soluble in water up to the extent of 3 per cent. An interesting feature about promacotin is that while it is not effective in experimental tuberculosis in guinea-pigs, it is effective in leprosy.

Toxicity.—Sharp and Payne (1948) state that in the body it does not break down into diamino-diphenyl-sulphone, and because of this it is reported to be less toxic than the other sulphone drugs which are considered to break down into the parent compound to varying extents. Johansen *et al.* (1950) reported uniform, universal and sustained clinical improvement in cases of leprosy following the oral administration of promacotin.

Dosage.—Starting with small initial doses, Johansen *et al.* (1950) gradually worked up the dose to 3 to 4 gm. a day. They found that the drug is well tolerated orally even on prolonged administration of these high doses.

Blood concentration.—Johansen *et al.* (1950) reported that promacotin blood level remained fairly constant between 1.5 and 2.0 mg. per cent on oral doses varying from 3 to 4 gm. daily, irrespective of the length of treatment. The urine concentration however behaved differently as the levels tended to increase with the increase in the duration of treatment, and eventually some patients were reported to excrete by the kidney as much as they were taking in by mouth.

Sulphetrone

General.—This compound is tetrasodium-phenyl-propylamino-diphenyl-sulphone. It is a cream-coloured material exceedingly soluble in water.

Reports of use in leprosy.—Harkness and Brownlee (1948) have reported that sulphetrone was first used in the treatment of leprosy in 1943 in a lepromatous case with nodules. Wharton (1947), Dharmendra and Chatterjee (1947), Dharmendra (1948, 1950), Davey (1948), Davidson (1948), Winter (1948), Cochrane (1948), Cochrane *et al.* (1949), Dharmendra, Dey, Bose and Kapur (1950) and Dharmendra, Sen and Chatterjee (1950) have reported on the beneficial effects of sulphetrone in the treatment of leprosy.

Toxicity.—Brownlee *et al.* (1948) from their experiments in animals found that sulphetrone is virtually non-toxic in the acute experiments, and has low toxicity in prolonged ones. They concluded that when given by mouth sulphetrone is the least toxic of the sulphones, and also less toxic than any of the sulphonamide drugs. They reported that in rabbit the chronic hæmato-toxic effects include a hæmolytic anæmia, an anæmia of iron lack, and an anæmia of nutritional origin. Brownlee (1948) reported that this was seen in man also. As a matter of fact hæmatological changes follow the administration of any of the sulphone drugs.

Absorption from the gut.—Sulphetrone as also diasone and the other sulphone derivatives given by mouth are very incompletely absorbed from the gut. Brownlee (1948) reported that although exceedingly soluble in water, sulphetrone is slowly absorbed from the intestinal tract. Smith (1949) reported that of the three sulphones (DDS, diasone and sulphetrone), sulphetrone was most incompletely absorbed from the gut; as much as 70 to 100 per cent of the daily oral intake of sulphetrone may be recoverable from faeces, only 11 per cent being recoverable from the urine.

Intramuscular administration.—The oral use of the sulphone drugs which are incompletely absorbed from the gut is not economical since a large amount of them passes out unabsorbed and is thus wasted. Parenteral administration of these drugs is therefore more desirable.

Dharmendra, Dey, Bose and Kapur (1950) have reported a detailed study of intramuscular administration of sulphetrone. They worked with 6 different preparations of sulphetrone—watery solution, suspensions in hydnocarpus and arachis oils with and without wax, and emulsion in hydnocarpus oil and water. They studied the absorption, excretion, height and maintenance of blood levels after varying doses of the different preparations and arrived at the following conclusions :

(1) As judged by the height of blood concentration produced after a particular dose, maintenance of blood levels and longest period up to which the drug could be detected in the blood, the dose by the intramuscular route would be less than 1/5th of the dose by the oral route.

(2) On the same considerations, as also because of ease of injection, the watery solution appears to be the best preparation, the emulsion in hydnocarpus oil and water being the next. The oily suspensions with or without the addition of wax offer no advantage since they do not possess any appreciable repository effect, but on the other hand these suspensions have certain disadvantages, as they are more difficult to inject and more likely to produce irritation, induration, etc., at the site of injection.

(3) The intramuscular administration of sulphetrone has a great advantage over the oral administration, as the intramuscular treatment is more economical and possibly more effective.

Dosage.—By the oral route the initial dose is 1 tablet 3 times a day (a total of 1.5 gm.) and this dose is gradually increased to a total dose of 12 tablets a day (6 gm. daily). At this rate the weekly dose for 6 days a week works out at 36 gm. per week.

By the intramuscular route a total dose of 4 gm. a week would suffice; this amount may be given in two doses of 2 gm. twice a week, or in smaller doses more frequently.

Blood concentration.—(a) After oral administration—Wharton (1947) reported that with an average daily dose of 3 gm. the blood concentrations of the drug vary from 6 to 12 mg. per cent. These figures appear much too high and are not in keeping with the findings of other workers. Dharmendra (1948) reported blood concentrations varying from 0.5 to 3 mg. per cent, on the average about 2 mg. per cent, and if the treatment is prolonged without rest, the blood concentration tends to be even lower. Smith (1949) on doses varying from 2 to 14 gm. a day obtained blood levels from 1.5 to 7.5 mg. per cent, on 3 gm. a day the concentration was 2 mg. per cent and on 6 gm. a day 2.5 mg. per cent.

(b) After the intramuscular administration—By the intramuscular administration of sulphetrone higher blood concentrations are found. Dharmendra, Dey, Bose and Kapur (1950) studied this question in detail. They found that the blood concentration was between 3 and 10 mg. per cent with the doses varying from 0.3 to 2 gm. of sulphetrone. The highest concentration was reached 2 to 3 hours after injection, and then it began to decline. Regarding the retention of the drug in the blood they found that after doses of 0.1 to 0.3 gm. the blood is practically free from the drug at the end of 24 hours; after doses of 0.6 to 1.5 gm. it is practically free from the drug at the end of 48 hours; and after a dose of 2 gm. it is practically free at the end of 72 hours.

In a study of two cases, Smith (1949) has reported unusually high concentrations after intramuscular administration of 2 and 4 gm. sulphetrone. His figures at one hour after injection were 26 and 40 mg. per cent for 2 and 4 gm. doses respectively. These figures are abnormally high and cannot be taken as representing the general state of things.

Diamino-Diphenyl-Sulphone

General.—This is the parent sulphone and is very sparingly soluble in water (0.01 per cent at room temperature and 0.05 per cent in hot water). Because of its great toxicity in doses of the order of 1 to 2 gm. a day, it was not used in the treatment of leprosy till recently. In recent years however successful trials have been carried out with very small doses of this compound, given both orally and parenterally by subcutaneous or intramuscular route.

Reports of use in leprosy.—Cochrane (1948) suggested subcutaneous injections of a 25 per cent emulsion in oil, and later Cochrane *et al.* (1949) reported on its use giving 5 cc. of this emulsion twice a week (2.5 gm. per week). They reported that this was the most active anti-leprotic drug but that in this dosage it caused toxic symptoms which were sometimes alarming. Molesworth and Narayanswami

(1949) also administered it parenterally, but used smaller doses, up to 1 gm. a week, without any loss of efficacy. Lowe (1950) has used it by mouth and he advocates working up to a standard dose of 300 mg. (0.3 gm.) a day. Dharmendra, Chatterjee and Bose (1950) have used both the intramuscular and the oral routes, and find that in the case of this drug the intramuscular route offers no special advantages. They are of the opinion that the dose of 300 mg. per day is rather high.

Toxicity.—Diamino-diphenyl-sulphone is reputed to possess a high degree of toxicity because of which it has not been used in the treatment of bacterial infections in man. Early experiences in animals demonstrated that its anti-bacterial activity is about a hundred times greater than that of sulphanilamide, but that its toxicity was also ten to twenty times greater. As stated earlier, Lowe (1950) quotes from a personal communication from Buttle saying that the therapeutic trials in human beings with doses of the order of 1 to 2 gm. a day produced methaemoglobinæmia and other toxic effects, and were therefore abandoned.

Of late, however, trials are being made of the use of the small doses (0.1 to 0.3 gm.) in the treatment of leprosy.

Absorption from the gut.—Unlike its derivatives DDS is quickly and completely absorbed from the gut. Lowe and Smith (1948) and Smith (1949) found that when given by mouth in doses from 0.1 to 0.4 gm. DDS is almost completely absorbed from the gut and is very slowly excreted in urine so that it is retained for a long time in the body. (Diasone and sulphetrone are incompletely absorbed from the gut and are quickly excreted in urine.)

Dharmendra, Chatterjee and Bose (1950) have confirmed and extended the findings of Smith using DDS both orally and parenterally. They found that when given by mouth it can be detected in blood five minutes after the administration of even a small amount (10 mg.) and that the drug is retained for long in the body and is very slowly excreted.

Intramuscular administration.—Dharmendra, Chatterjee and Bose (1950) have compared the intramuscular and oral administration of the drug. They found (1) that when given by either route it can be detected in blood within five minutes of administration of even a small amount (10 mg.), (2) that with either route the different doses give rise to similar ranges of blood concentration, and (3) that after either route the drug is retained for long and is very slowly excreted, the retention being a little longer after the intramuscular administration. From these observations they conclude that unlike sulphetrone the intramuscular administration of DDS has no advantage over the oral route.

Dosage.—Cochrane *et al.* (1949) used 2.5 gm. per week intramuscularly in two equal doses, but found that in this dose the drug produced toxic symptoms which were sometimes alarming; they advocate a dosage of not more than 1.5 gm. per week. Molesworth and Narayanswami (1949) have also used the drug parenterally in doses up to 1.0 gm. a week. Lowe (1950) has used it by mouth and he advocates a daily standard dose of 300 mg., the initial dose being 100 mg. a day and gradually raised to the 300 mg. in the course of five weeks. He however hints at the possibility that the standard dose may turn out to be less than the 300 mg. per day. In his later extensive work Lowe (personal communication) is using a maximum daily dose of 200 mg. for six days a week; he is also using a dose of 400 mg. twice a week.

Dharmendra, Chatterjee and Bose (1950) have used the drug by both the oral and intramuscular routes and find that, in case of this drug, the intramuscular administration offers no advantage. They are of the opinion that a dose of 300 mg. per day is rather too high, and that the maximum safe dose would be about 200 mg. daily (1.2 gm. a week). Muir (personal communication), who has used the drug by the oral route, is also of the same opinion.

It may be concluded that the dose of DDS would be about 1 gm. a week, that this dose should be worked up gradually beginning with smaller initial dose, and that intramuscular administration does not appear to offer any special advantages.

Blood concentration.—Smith (1949) has reported that on oral doses of 0.1 to 0.4 gm. (100 to 400 mg.) a day, the mean minimal blood concentration varies from 0.4 to 1.5 mg. per cent according to the dose, it being 1 mg. per cent on a dose of 300 mg. Cochrane *et al.* (1949) found that the blood concentrations ranged between 0.7 and 2.0 mg. per cent, and they suggest that it should not be allowed to rise above 2 mg. per cent. Lowe (1950) has reported that on daily doses of 0.1 to 0.5 gm. (100 to 500 mg.) the blood level varies from 0.5 to 2.2 mg. per cent according to the dose, it being 0.8 to 1.4 mg. per cent on a dose of 300 mg. On the assumption that the proprietary sulphones are partly broken down to DDS in the body, and that the therapeutic activity of these drugs depends upon the DDS released, he concludes that the minimum therapeutic blood level of DDS in leprosy is perhaps 1 mg. per cent or even less. Dharmendra, Chatterjee and Bose (1950) found that with doses varying from 50 to 300 mg. per day, the blood concentration varied between 0.4 and 1.8 mg. per cent according to the dose. 200 mg. per day produces a minimal blood concentration of 1 mg. per cent. the maximum

being about 1.5 mg. per cent. They also found that blood concentrations with the various doses were more or less similar irrespective of the route of administration—oral or intramuscular.

Mode of Action of the Sulphones

All the sulphone drugs used in the treatment of leprosy have been found to be effective, and it is very likely that the active radical in all the cases is the same. Many workers believe that the activity of the proprietary sulphones is dependent on their degradation in the body into the parent substance (DDS), and that the effective dose of a proprietary preparation depends upon the extent of this degradation. There are some other workers, however, who do not agree with this view in respect of certain proprietary preparations.

Feldman, Hinshaw and Moses (1940) referred to the possibility that promin and diasone may be broken down in the body to DDS or to a similar substance common to all. They stated that there was no proof that breakdown occurred, but that the union between the parent substance and the added radicals appeared to be unstable. Johansen and Erikson (1948) stated that it appeared, though not definitely established, that diaminodiphenylsulphone, the chemical group common to all the drugs, is the active principle. Smith, Jackson, Junge and Bhattacharya (1949) and Smith, Jackson, Chang and Longnecker (1949) stated that there was evidence to indicate that promin, diasone and possibly sulphetrone are metabolized in the body to the toxic parent substance. Smith (1949) extracted DDS from urine of patients undergoing treatment with diasone and sulphetrone, and concluded that this provided evidence for the partial hydrolysis of these compounds in the body.

On the other hand, Brownlee *et al.* (1948) state that sulphetrone is not hydrolysed to DDS in the body, and Sharp and Payne (1948) make a similar statement regarding promacutin. However, it appears that Brownlee has slightly changed his views and now believes that in case of sulphetrone there is a small amount of hydrolysis, as is evident from the following quotation made by Lowe (1950) from a personal communication to him from Brownlee: 'It appears most likely to us that it is the rate of degradation (to D.A.D.P.S.) that is important; that is to say, that the lack of toxicity of sulphetrone could quite well be consistent with a slow hydrolysis to D.A.D.P.S.' After quoting from another personal communication from Brownlee, Lowe concludes: 'Thus even according to Brownlee, who appeared to be the chief exponent of the opposite view, complex sulphones possibly or probably act by being hydrolysed to D.A.D.P.S., though with some of the complex sulphones the amount of this hydrolysis is very small.'

Regarding the ultimate mode of action of the active principle of the sulphone drugs there is some uncertainty. It appears that they have a bactericidal or bacteriostatic action on the leprosy bacilli, though this cannot be proved, since neither the leprosy bacilli can be grown in laboratory media, nor any experimental animal is known to be susceptible to it. All the same, this seems likely, and the use of the sulphones in leprosy is based on their action on another acid-fast bacillus—the tubercle bacillus—in *vitro* and in experimental animals. The probability of a direct action of sulphones on the leprosy bacillus is supported by the morphological changes in the bacilli and the reduction in their number seen in cases under prolonged sulphone treatment. Faget *et al.* (1946) summarizing their five years' experience with promin therapy expressed the view that it appeared to have a chemotherapeutic effect on the leprosy bacillus. In this connection they referred to the 'important finding' of Fite and Gemar (1946), 'that promin appears to eliminate bacillary infection of the blood vessels and blood stream, thereby preventing the formation of new lesions'. Lowe (1948), who also holds the view that sulphones have a direct effect on the bacilli, considers that the findings of Fite and Gemar (1946) are 'probably true, but it would appear not to be the whole truth'. According to him 'it appears probable that sulphone is taken up by tissue cells, particularly reticulo-endothelium, including the actual cells of the leprosy lesions, and that it exercises an influence on the bacilli in the lesions, which are mostly intracellular'.

However, the persistence of the bacilli for a number of years during sulphone treatment, even though in decreasing number, is a fact, which is apparently difficult to reconcile with the view that the sulphones have a direct action on the bacilli. But the presence of enormous number of bacilli in the body of a lepromatous case, together with the fact that in experimental animals injected with killed lepra bacilli, the dead bacilli are known to persist for long, would seem to offer a plausible explanation for this long persistence of the bacilli in cases under sulphone treatment. Lowe (1948) considers that 'it is not impossible that these persisting bacilli are dead, although this cannot be proved'.

Clinical Results

All the sulphone drugs have produced similar results, and they will, therefore, be considered together. These drugs have mostly been used, and rightly so, in the treatment of the more serious, *i.e.* the lepromatous type of cases. Of late, however, they have been used to a limited extent in the treatment of the 'neural' or 'tuberculoid' cases with good results. The results in the two types of cases will be described separately.

(a) *Results in the lepromatous cases.*—Beneficial results are seen in all lepromatous cases, but they are more manifest in the advanced cases with extensive thickening, nodulation, ulceration, and lesions of the eyes, nose and throat.

The first thing to be noticed is that further progress of the disease is checked, and this is most apparent in the patients who have been progressively going downhill either without any treatment or on treatment with hydnonearpus oil. Next the disease begins to retrogress slowly but surely. For any appreciable objective improvement one has to wait for at least about 6 months, but in a few weeks of treatment the patient begins to have a feeling of well-being and lightness. The first signs of improvement are observed in the healing of ulcers in the skin, and nose and clearing up of the lesions in the eyes, nose and throat. In time the whole appearance of the patient and his outlook towards life are changed; in place of the mask-like expressionless face, he comes to possess a face with expression and features; and instead of having a sense of frustration, he is full of hope. The general health of the patient improves considerably. The marked all-round improvement is usually seen after treatment for about 1 to 2 years.

The clinical improvement seen in the various signs and symptoms may be summarized as under :—

Leprous ulcers.—Chronic leprosy ulcers heal rapidly and do not recur. The healing of the ulcers provides the first objective sign of improvement and contributes considerably to the welfare of the patients.

Nasal mucosa.—The improvement in the nasal condition is evident before long. The blocking of the nose gradually clears up, and epistaxis, if any, stops; nasal ulcers heal though a little more slowly than the ulcers on the extremities.

Eye reaction.—Leprosy iritis and eye reaction respond very well to treatment. The pain and redness in the eyes become much less and gradually disappear, and the eye reactions are progressively controlled. With the improvement and settling down of the eyes it is possible to undertake in suitable cases such operative measures as iridectomy and removal of an opaque lens, measures which improve and restore eye-sight, but which cannot normally be considered in an eye subject to frequent flare-ups.

Larynx.—The lesions of the larynx gradually heal under treatment, and hoarseness of voice due to involvement of the larynx improves greatly. In patients with symptoms of acute tracheal obstruction and in whom tracheotomy might seem imminent, the sulphones quickly improve the situation, and the patients are

saved from tracheotomy. Sloan (1948) has reported that 'improvement of laryngeal lesions is one of the most striking results of sulphone treatment, perhaps the most striking one'. He found the drugs of great value in patients with lepromatous laryngeal involvement; in a number of patients it was possible to remove tracheal tubes that they were already wearing, and in a few others tracheotomy was avoided.

Nodulation and infiltration.—Nodulation and thick infiltrated areas in the skin begin to shrink shortly after treatment. The rate of subsidence is no doubt slow but the results are certain. In some cases the nodules soften, burst, discharge and then cicatrize. In others the nodules are absorbed without any matter being discharged. In both instances after prolonged treatment one can find only scars in place of previous nodules.

Towards the latter part of treatment a number of patients who are otherwise improving become subject to the appearance of temporary short-lived small nodules or raised patches. These tiny patches or nodules may be few or numerous and usually appear in crops; they do not last for long and subside usually within a week. In most cases they are a little painful. They are not confined to the patients who initially had leprosy nodules and thick patches but are about equally frequently seen in the patients who initially had only generalized diffuse infiltration without nodulation. The appearance of such nodules has been reported by Wolcott (1947), Souza Lima (1948), Souza Lima and Rath de Souza (1949) and Dharmendra (1950). The exact significance of these nodules or patches is not clear but perhaps they indicate a change for the better in the defence mechanism of the patient against the leprosy bacilli.

Caseating lymph glands.—Dharmendra (1950) has reported the subsidence of large swollen and caseating lymph glands in a number of patients. These glands were found in cervical, axillary and inguinal regions and were of long standing; in some cases they had burst and given rise to chronic deep sinuses. Under sulphone treatment the glands subsided rapidly, and the sinuses healed gradually, leaving behind depressed scars. In the pre-sulphone days such a progress was unthinkable.

Lepra reaction.—Leprosy is a chronic disease in which rapid changes are not usually seen, but occasionally acute exacerbations occur, and this acute flare-up is termed 'lepra reaction'. During the period of reaction the patient gets fever, the old lesions increase in size and thickness, new lesions appear, and there is increase in the eye symptoms, or the eyes may be involved for the first time during reaction. Under sulphone treatment 'reactions' become less frequent and less severe, and finally are completely eliminated. The sulphones not only

prevent or minimize the occurrence of reactions but have been actually beneficial for these reactions if given in small doses during the reaction (Dharmendra, 1950). In some cases these drugs first precipitate reactions which are then followed by improvement.

Nerve pains.—Improvement in this condition is very slow, and it is only after prolonged treatment that improvement is seen.

Bone pains.—Under treatment bone pains disappear in most cases. This is possibly due to healing of leprosy lesions in the bones. Erickson and Johansen (1948) have reported on the 'Bone Changes in Leprosy under Sulphone Therapy'. They have concluded 'that lesions in bones presumably due to the direct action of *M. lepra*, such as cysts, heal; and that a restraint on further progression of atrophic bone absorption, secondary to neural involvement probably occurs'.

Deformities.—The already existing deformities are not benefited by sulphone treatment, but because of the healing of the nerve lesions the tendency to further deformities is checked.

(b) **Results in the neural cases.**—It is difficult to assess the effects of sulphones in the neural cases of leprosy because of the relative benign nature of the disease in this type, and the tendency to spontaneous cure seen in several of the cases. However, there is some evidence that the sulphone drugs are of value in the treatment of active lesions of this type of disease. Cochrane (1949) was definitely against the use of the sulphone drugs in the active neural cases—tuberculoid or simple maculo-neural. His views on the subject were as below:

'There is an accumulating evidence to show that there may be an exacerbation of the disease in the initial stages of this therapy. Therefore in the case with neural macules there is a potential liability for it to pass into the lepromatous stage. Admittedly this will recover under further sulphone therapy, but we are not sufficiently sure of our ground deliberately to do this or run the risk of doing it. Even though no such result follows it is almost impossible to estimate the improvement in the case with neural macules because there is no yard-stick by which to measure improvement.

'In the tuberculoid case I am of opinion that sulphone therapy is decidedly harmful because it is liable to precipitate an acute tuberculoid reaction with all the dangers of nerve damage through inflammatory reaction in the nerves possibly leading to abscess formation.'

Later, he (Cochrane, 1949a) seems to have modified his views as under:

'The question of treating active neural cases—tuberculoid or simple maculo-neural—with the sulphone is still *sub judice*. I am strongly of the

opinion that in such cases definite results have to be obtained within six months to be of any significance regarding the value of the drug which is being used. Because of the difficulty of assessing the activity of the drug in neural cases, and also because the possibility of producing sulphone-resistant *M. lepræ* cannot be excluded, it is advocated that at present, except for experimental purposes, the sulphones should not be administered as a routine in neural cases.'

Souza Lima (1948) treated cases of this type with 'cutaneous manifestations of from 5 to 10 years' continuous progression and subject to repeated outbreaks of tuberculoid lepra reaction. After the intensive sulphone therapy the patients became free from attacks of the reaction and after 12 to 20 months of treatment there was either disappearance of all the cutaneous lesions or return to the original uncharacteristic appearance'. Lowe (1950) reported on the beneficial effects of sulphone treatment in the tuberculoid type of cases. Under this treatment inflammation and thickening of the patches in the skin tend to subside in a matter of few weeks and its effect on the thickening and inflammation of the nerves is already apparent in most cases after treatment for a few months. Dharmendra, Sen and Chatterjee (1950) report on the treatment of the active tuberculoid lesions mostly in the stage of reaction; in some of the cases the patients were subject to repeated and frequent reactions and in a few of them these attacks were not controlled by the usual treatment for these conditions. Under sulphetrone treatment the reactions were controlled in all the cases within a few weeks of treatment, and the skin patches subsided and became flat in a few months of treatment. The rate of subsidence of the lesions in these cases was much quicker than could be expected under treatment with hydnocarpus oil or on account of spontaneous recovery. Johansen *et al.* (1950) had one case of tuberculoid type amongst the patients treated with promacatin. This patient improved markedly and rapidly. Allowing for the tendency to spontaneous improvement, these authors believed that 'the rapidity with which the lesions regressed in this case' suggested that promacatin contributed to this improvement. They concluded that:

'The opinion expressed by some that sulfones are of no value in tuberculoid leprosy is probably influenced by the feeling that this type of leprosy is not in need of treatment. The improvement noted in the patient of this type treated with promacatin was certainly more striking and rapid than that usually observed without treatment.'

It can be concluded that sulphones are not harmful in the neural cases of leprosy, and that they are indicated in 'certain stages' of the disease. The special indications for the use of the sulphones in such cases appear to be (1) the

occurrence of frequent reactions, (2) the presence of leprosy bacilli in the lesions, and (3) the continued progression of the disease, although the routine smear examination may not show the presence of leprosy bacilli (bacilli in sections are found in a considerable number of such lesions).

Bacteriological Improvement

The bacteriological improvement is slow and not as apparent as the clinical improvement. The first change to be seen is not the reduction in the number of bacilli but the morphological change whereby the bacilli become less acid-fast and stain irregularly. Gradually there is seen a reduction in the number of bacilli, but it takes a very long time for the bacilli to disappear completely. Any appreciable reduction in the number of bacilli is not seen till the second year of treatment, and the number of patients who become bacteriologically negative is small in the second year, bigger in the third year and continues to rise in subsequent years of treatment. It may be said that it takes about five years to make most patients negative.

It can, therefore, be said that bacteriological improvement though slow is quite definite. An important observation in this connection is that the nasal smears become negative much earlier than skin smears taken from different parts of the body. This observation together with the fact that leprosy ulcers both in the skin and the nose heal rapidly under sulphone treatment have a bearing on the rôle that the sulphone drugs can play in the control of the spread of leprosy, and this matter is discussed later.

Toxic Effects and Complications

Most of the workers who have used the drugs in the treatment of leprosy agree that marked toxic effects or complications are seldom seen. Dharmendra (1950) reported that in cases treated for 1 to 3 years with sulphetrone orally and intramuscularly, no evidence of damage to liver was obtained as judged by the tests for the presence of the urobilin and urobilinogen in urine and the van den Bergh test; only occasionally have these tests been positive in a few cases. Smith (1950) found no evidence of liver damage in cases treated for 6 to 10 months with daily doses of 0.3 gm. DDS or 5 to 6 gm. sulphetrone. He used the following procedure for testing the liver function: palpation for enlargement of liver, alcohol turbidity test for the gamma globulin, van den Bergh test for plasma bilirubin, test for urobilin in urine, and hippuric acid test for measuring the detoxicating power of liver.

Minor degrees of toxic effects are frequently seen specially in the earlier part of the treatment. These include nausea, gastric upsets, burning sensation in hands and feet, giddiness,

weakness and palpitation. These symptoms disappear as the treatment is continued.

In some cases an increase in dose is sometimes accompanied by an attack of neuritis, synovitis or iritis. These conditions however settle down quickly when the dose is reduced or the drug temporarily suspended.

Exfoliative dermatitis is seen in a small number of cases but it responds quickly to treatment with calcium and vitamin B. Drug sensitization is sometimes seen as evidenced by appearance of urticarial rash after the injection. The patients can be desensitized by repeated injections of minute quantities.

Although the sulphone drugs are effective in ultimately controlling the lepra reaction (acute exacerbation) not infrequently seen in cases of leprosy, sometimes they bring about a reaction specially if the initial dose be big or if the dose be increased quickly. Another feature which has been observed is that in cases which are otherwise improving, one sometimes sees appearance of small short-lived nodules or thick patches. In the writer's experience this has been most common in the patients treated with diamino-diphenyl-sulphone. Wolcott (1947) considered it highly probable that the appearance of these lesions offers a definite indication of the resistance of the host. Souza Lima (1948) described this phenomenon as 'pseudo exacerbation' as he thinks that the appearance of these temporary lesions is an indication of the changed reaction of the tissues of the patients.

The one constant toxic effect that the sulphones produce is a fall in hæmoglobin and red blood corpuscles. However, the anæmia is not usually of a serious nature, and only in a small percentage of cases necessitates temporary withdrawal of the drug, and in only a rare case with a poor initial blood picture has it to be discontinued permanently. In the earlier part of the treatment in most cases there is a fall in hæmoglobin and R.B.C. values, but as the treatment continues the blood level rises to its initial or even higher level with hæmatinics. Dharmendra (1948, 1950) has reported a number of cases in which the blood picture was well maintained even after 2 to 3 years of sulphone treatment. In the patients with initially poor blood condition he reported actual improvement with small doses of sulphetrone.

Procedure of Treatment

Treatment to be regulated by blood examinations.—Before starting treatment with the sulphone drugs a blood examination should be made specially for total red blood cell count and hæmoglobin estimation. If the red cells and hæmoglobin are much below normal, say, below 75 per cent, the patient should be put on a course of hæmatinics, and the treatment with

sulphone drugs should be started only after the blood picture has improved satisfactorily. In cases with a poor blood picture where there are urgent indications for treatment with sulphones the writer has obtained very good results with small doses (0.3 gm.) of sulphetrone given intramuscularly.

During the course of treatment periodic blood examination should be made and hæmatinics given if indicated by the results. For the purpose of periodic blood examinations hæmoglobin estimation would be sufficient since the fall in red blood cells and hæmoglobin is parallel; a full blood examination may be done only occasionally.

Dose to be gradually increased.—It is the usual practice to commence the treatment with a small initial dose, and to increase it only gradually according to the tolerance of the patient. By this method untoward symptoms and serious reactions are minimized. Coelhrane, however, believes that this procedure is likely to result in the drug resistance of the leprosy bacilli. While this is possible, there is no evidence that it takes place, and Johansen and Erickson (1948) state that this possibility is more apparent than real, and that they have not come across evidence of drug fastness throughout their long experience with the use of sulphone drugs.

Periods of rest.—During the course of treatment the patient should get periodic rest when no treatment with the sulphones should be given. This will minimize the chances of severe toxic symptoms and will give time to the hæmopoietic system to recuperate. During each week of treatment the patient is rested for a day so that he gets treatment for 6 days in a week. Treatment for a number of weeks should be followed by rest for a few weeks, 4 weeks of treatment may be followed by 1 week's rest, or perhaps better the period of both the treatment and rest may be doubled so that the patient gets treatment for 2 months with a rest for about 2 weeks.

Choice of the preparation.—The sulphone drugs used in the treatment of leprosy have been described earlier. Of these promin, diasone and sulphetrone have been most commonly used, and of late DDS has come into the picture.

Of the three proprietary sulphones, promin was the first to be used in the treatment of leprosy, but it is also the most toxic. Because of its high toxicity by mouth it has to be given intravenously, with the result that although it produces high blood concentrations it is excreted very quickly and practically no drug remains in the blood some hours after the injection. There is not much to recommend it in preference to the other proprietary sulphones; it may, however, be preferable for a short period where symptoms are urgent and initial high

blood concentration are considered useful, such as in the case of an acute laryngeal obstruction where tracheotomy may look imminent. In such cases treatment may be started with intravenous administration of promin, and later continued with other preparations given by mouth or intramuscularly.

Both diasone and sulphetrone are well tolerated by mouth but diasone is absorbed better from the gut. For oral administration therefore diasone appears to be slightly better and preferable than sulphetrone.

Sulphetrone appears to be the least toxic, but it is very incompletely absorbed from the gut, and therefore the method of choice to administer this drug is by the intramuscular injection of a 50 per cent aqueous solution.

In comparison with the proprietary sulphones, DDS is quickly and completely absorbed from the gut, is retained in the body for long periods, and is the least expensive. However, it is also the most toxic, and but for its toxicity this would have been the sulphone drug of choice, specially when there is some evidence to the effect that proprietary sulphones are active by virtue of their being broken down in the body partly to DDS. Moreover, because of its low cost this would be the drug for the routine treatment of the very large number of cases in endemic areas with bad economic conditions. However, because of its toxicity its extensive use is not to be recommended at the present stage and when used the dose should not exceed 200 mg. a day.

DDS has been used both by mouth and by injection of a 25 per cent suspension in oil with wax. Because of the almost complete absorption of the drug from the gut the parenteral administration of DDS does not appear to have any advantage. Lowe (1950) is also of the same opinion. Since even small doses produce anaemia necessitating treatment with hæmatinics, there is much to be said for the inclusion of iron and vitamin B in the same tablets with DDS. This is possible because of the very small dose of DDS to be administered, and it would simplify matters and make the overall treatment cheap which is so essential for any method of treatment meant for the millions.

It may be concluded that in the writer's experience the parenteral administration of sulphetrone is so far the safest, effective and at the same time inexpensive method of treatment with the sulphone drugs. The treatment with DDS will be cheaper but because of its greater toxicity, at the present stage it cannot be recommended as a routine method of treatment except in institutions where the patients are under observation. Lowe (personal communication) is using it on an extensive scale in Nigeria, where over a thousand patients are under DDS treatment in leprosy colonies and

isolation villages and before long several thousands more are expected to be included.

Rôle of Sulphones in Controlling the Spread of Leprosy

If the bacteriological improvement under the sulphone drugs were as rapid as the clinical improvement, these drugs would have contributed greatly towards the control of the spread of the disease. The bacteriological improvement, however, is very slow, treatment for 4 to 5 years or longer being usually necessary to render a patient bacteriologically negative.

All the same, the sulphone treatment, if extensively applied, is sure to make an impression on the problem of the prevention of the spread of leprosy. The treatment no doubt takes long to make all the bacilli disappear from the patient's body, but all the same the bacteriological improvement is evident after treatment for a year. This improvement appreciably decreases the infectivity of the patient. The reduction in infection is caused not only by an actual decrease in the number of bacilli, but also to a great extent by the healing of the leprosy ulcers both in the nose and other parts of the body, which considerably reduces the infective discharges from the patient. Another factor that has a bearing on the matter is that nasal smears become negative early in the course of treatment, even at a time when smears from other parts of the body show a moderate number of bacilli. Discharges from the nose and from the ulcers are undoubtedly the most potent sources of spreading the infection, and any measure which minimizes these sources is sure to have a restraining influence on the spread of the disease. However, for this influence to be demonstrable sulphone therapy has to be applied on an extensive scale.

A Plea for the Use of Sulphone Drugs on a Wider Scale

The sulphone drugs are now well established in the treatment of the more serious cases of leprosy and should no longer be considered in an experimental stage. All the same these drugs are being used in India in a very limited scale. This is mainly because of the fact that the proprietary sulphone drugs are very expensive specially since the treatment has to be continued for several years. The cost of proprietary sulphone drugs for one patient for one year would work out at about Rs. 250.

Efforts have been made to reduce the cost of treatment and these have been mainly in two directions, viz (1) the parenteral use of the proprietary sulphones so far used by mouth and (2) the use of small doses of the parent compound (DDS), which in the usual doses is highly toxic. Investigations of the first nature have been carried out with sulphetrone and it has

been found that when given by the intramuscular route the amount of sulphetrone needed is much less than that by the oral route, and that the cost of the drug for one patient for one year would be about Rs. 30. Thus in the leprosy institutions where the giving of injections should entail no extra expense, the cost of treatment can be cut down to about 1/10th of that by the oral route.

The other direction, in which efforts to reduce the cost of treatment with the sulphones have been made, is the use of the parent compound (DDS). With it the annual cost of the drug for one patient for one year would be less than Rs. 20. This drug should, however, yet be considered in an experimental stage and should not be used on an extensive scale till the dose is well standardized, since even in the small doses the writer finds it more toxic, and more liable to precipitate reaction than the proprietary sulphones in their usual doses.

As already stated earlier the sulphone drugs are of remarkable value in the treatment of serious type of leprosy, it is only desirable that the largest possible number of suitable patients should get the benefit of this treatment. It is specially indicated in advanced patients with chronic ulcers and lesions of the eyes, nose and throat. All such patients should as far as possible be given the benefit of sulphone drugs. Even if it is not possible to give a prolonged treatment with these drugs, the patients with pressing symptoms should be treated with these drugs for a short period of, say, six months or one year, when they can revert to the treatment with hydnocarpus oil. This is suggested because definite improvement in ulcers and lesions of the mucous membranes is seen after treatment for about six months.

It is not only in the interest of the individual patients that the wider use of the sulphones is advocated, but the wide application of these drugs is likely to have a favourable impression on the whole anti-leprosy problem. For example, its large-scale use in the leprosy institutions can result in a quick turn-over of patients, and this would lead to a better use of the available accommodation in the institutions—a thing so badly needed in a country like India, where the in-patient accommodation is grossly inadequate to meet the needs. Under the sulphone drugs the infectivity of the patients is considerably reduced at the end of one year or so; at this stage the patients could be discharged to continue their treatment as out-patients and to make room for other highly infectious cases.

As stated earlier the extensive use of the sulphone drugs in the leprosy institutions as also on out-patients is likely to make a definite contribution towards the control of the spread of leprosy.

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Medical News

The following 3 items are reproduced from releases issued by Pan-American Sanitary Bureau, Regional Office, World Health Organization, 2001 Connecticut Avenue, N.W., Washington 8, D.C. :—

(1) PAN-AMERICAN SANITARY BUREAU SENDS TYPHUS VACCINE TO AFGHANISTAN

(Washington, 13th June)

THE Pan-American Sanitary Bureau, Regional Office in the Americas for the World Health Organization, this morning shipped by air from New York to New Delhi, India, 27,383 cc. of anti-typhus vaccine. This vaccine is destined for Afghanistan where a serious effort is being made by the Afghan government to conquer recurrent outbreaks of louse-borne typhus.

Request for the vaccine was made by the W.H.O. Regional Office in New Delhi to W.H.O. Headquarters in Geneva. Geneva headquarters, in turn, instructed the Pan-American Sanitary Bureau to ship the required supply of vaccine. The first shipment was made on 29th May. To-day's shipment left at 8-30 this morning and will reach New Delhi on Thursday afternoon.

(2) W.H.O. TO SPONSOR INTERNATIONAL SYPHILIS SEMINARS IN HELSINKI AND PARIS NEXT SEPTEMBER

(Geneva, 16th June)

Two international syphilis seminars bringing together American and European specialists will be held next September in Helsinki and Paris, under the auspices

of the World Health Organization, to promote the exchange of information on numerous aspects for the prevention, diagnosis and treatment of syphilis.

The agenda of these meetings includes the treatment of nervous, early and congenital syphilis, the sero-diagnosis of syphilis, technical orientation, laboratories, and antigen production. Participants will review the results of the World Health Organization United Nations International Children's Emergency Fund campaign against congenital syphilis through penicillinotherapy. These campaigns are now under way or in preparation in many countries of Europe, Asia, America and the Eastern Mediterranean.

The Helsinki seminar, to be held from 4th to 10th September, will include from 20 to 25 specialists from Denmark, Iceland, Norway, Sweden, the United States and Finland.

The Paris meeting, to be held from 25th September to 7th October, will include specialists from Belgium, Greece, Ireland, Italy, Luxembourg, The Netherlands, Portugal, United Kingdom, United States, Switzerland, Yugoslavia and France.

These meetings are also expected to provide useful guidance to workers on early syphilis. Demonstrations on the treatment of early syphilis with penicillin are presently under way with help from the World Health Organization at several university clinics in Europe and North Africa.

(3) PAN-AMERICAN SANITARY BUREAU OFFICIAL CONFERS WITH HEALTH AUTHORITIES IN SOUTH AMERICA

(Washington, 21st June)

Dr. Benjamin D. Blood, Chief of the Veterinary Public Health Section of the Pan-American Sanitary Bureau, Regional Office of the World Health Organization, has recently returned from South America where he discussed with health authorities in Argentina, Brazil, Uruguay and Chile the problems of controlling and eradicating animal diseases affecting man, such as hydatidosis, brucellosis and rabies.

The Bureau is studying the possibility of developing a programme of international co-operation in a campaign against these diseases.

SCORPION STINGS ARE FATAL IN TRINIDAD

In the course of his trip, Dr. Blood stopped in Trinidad where he learned that scorpion stings are the fourth largest cause of infant mortality on that island. Following a consultation with the Trinidad health authorities, Dr. Blood agreed to obtain a supply of anti-scorpion serum from the Butantan Institute in Sao Paulo, Brazil. This Institute produces serums against the venom of snakes, tarantulas and other spiders, and scorpions. The health authorities of Trinidad will test the serum for its effect on the venom of the Trinidad variety of scorpion. Dr. Blood also arranged for scorpions to be sent to the Butantan Institute to check the species. Should the available serum prove ineffective for that species, the Butantan Institute will then develop and produce a special serum for use against the venom of the scorpions in Trinidad.

BRAZIL'S SNAKE FARM

By ARTHUR R. PASTORE, JR.,

Special UNESCO Writer

(Reproduced from UNESCO Features, No. 22, 1st June, 1950, p. 11)

RECENTLY, a frightened, young Brazilian plantation worker was bitten by a snake. By all odds, he should have been dead in a matter of hours, for the snake was a poisonous one. Instead he was quickly called

for and rushed from his *fazenda* (farm) in a green bus bearing the name : Institute Butantan.

All within minutes after his arrival at the hospital of the Butantan Institute near Sao Paulo, the injured man was ushered into a room containing a long row of slender, glass tubes, each with a specimen of a poisonous snake. With his good arm, he pointed to the 'brother' of the one that had bitten him from this 'Rogues Gallery' of the reptile world. The proper serum was administered immediately and the young man's life was saved. To-day he is back at his job, thanks to the staff of Brazil's Butantan Institute, who have made remarkable strides in beating one of mankind's quickest killers, snake-bite.

This case is typical of the thousands the Institute has handled over the years. Besides medical treatment, the Institute has become world famous for its research on snakes and other tropical diseases such as cholera, plague and leprosy. Sera and anti-toxins produced in its laboratories are shipped to all corners of the globe as a public service.

Labels from the Institute's Shipping Room read like a world atlas—Bombay, Capetown, Manila, Shanghai, Cairo. . . . If an epidemic breaks out in Hong Kong, Butantan's vaccines are quickly sped to the scene by plane. If a request comes in for sera that must get to Rio, it's flown there inside of an hour. Speed and skill, plus the latest research techniques are the tools which Butantan's staff use to combat diseases and ills which have plagued mankind for centuries.

Located over 2,500 feet high in the hills outside Sao Paulo, the Butantan Institute takes in an area of over 1,000 acres, on which are located modern, air-conditioned laboratories, hospitals, museums, and other scientific research buildings—but the most important of all is the Snake Farm, the largest of its kind in the world.

In pillbox-like huts, are kept over 25,000 snakes of all kinds, poisonous and non-poisonous, which are used for study and experimentation. The 50,000 visitors, who flock to the Snake Farm each year, gasp in amazement as they see a dozen rattle-snakes sunning themselves or a giant python coiled around a tree. The snakes are under the care of experienced keepers and trainers, whose working clothes consist of riding breeches and long hip-boots. With apparent ease, a keeper casually seizes an eight-foot rattle-snake, holds open his jaws, and carefully milks the fangs for poison venom, which is deposited in his tray of vials, which will soon go back to the laboratory to be used serum.

In addition to the many varieties of snakes, there is a museum devoted to the study of all kinds of poisonous animals. Natural history exhibits show deadly insects like Black Widow Spiders, Scorpions, Gila Monsters and many of the world's other poisonous killers.

Nearby is a stable and pasture land, where roam a troop of specially bred horses, used for experimentation in developing new anti-toxins and vaccines to combat other deadly diseases. Thousands of people scattered all over the world owe their lives to the preventive medicine techniques of Butantan's trained staff of over 300 workers.

As you walk through the laboratories, you meet doctors and experts in many highly specialized fields. The grey-haired doctor in the corner, holding a beaker over a Bunsen burner, has devoted 30 years to the study of tropical medicine. In another section, is a research chemist who before the war was one of Germany's greatest technical experts in his field, heading the staff of a large Berlin hospital. Next to him is a young biochemist from China, who is learning his speciality at the Institute, so that he can go back to his own native land, armed with the latest scientific knowledge. And, so it goes, at Butantan you hear perhaps a half dozen languages spoken, but the language of science is universal.

This year, the Butantan Institute celebrates 50 years of progress. The idea of the Institute and its accompanying Snake Farm was the dream of Dr. Vital Brazil, who started the work a half century ago.

Dr. Brazil's work first came into the public eye several years ago when he was attending an international conference in the United States. At that time, an attendant at the Reptile House of New York's Bronx Zoo was bitten by a rattle-snake. All efforts to save him appeared useless, until Dr. Brazil was called in by the hospital to administer a vial of anti-toxin, taken from a Brazilian snake of the same species. The man's life was saved. Newspapers and press services reported the incident and, for the first time, Sao Paulo's Snake Farm was known the world over.

To-day, 84-year-old Dr. Brazil has retired from the Institute, but he still keeps a paternal eye over the Snake Farm, which has done so much to combat the once-high death-rate from snake-bite and other deadly diseases.

SEVENTIETH BIRTHDAY OF

DR. HELEN KELLER

(Reproduced from UNESCO Features, No. 23, 15th June, 1950, p. 10)

ON 27th June, Dr. Helen Keller will celebrate her seventieth birthday. Dr. Keller, deaf, blind and once mute, has been dependent since the age of 19 months on her sense of touch alone. Her teacher, Anne Mansfield Sullivan, whose ability was almost as exceptional as that of her pupil, first taught her words by putting an object such as a doll in her arms and then spelling the word DOLL slowly on her hand. Under her teaching, and with instruction at special schools for the deaf, dumb and blind in the United States, Dr. Keller not only learned to read, write and talk but became exceptionally proficient in her studies. Her case is the most extraordinary ever known in the education of blind deaf-mutes, her acquisitions including several languages and her general knowledge being wide. She has written several books, and takes a deep interest in methods of educating defective persons.

At a special session of the recent International Braille Conference at UNESCO House, Paris, held in her honour, Dr. Keller addressed the delegates on their work to create a universal Braille system for all different language areas of the world.

[For further details of the life of this remarkable woman, see *I.M.G.*, Vol. 84, January 1949, p. 15.—Editor, *I.M.G.*]

UTTAR PRADESH MEDICAL COUNCIL

MINUTES OF THE MEETING OF THE UTTAR PRADESH MEDICAL COUNCIL HELD AT LUCKNOW ON TUESDAY, 9TH MAY, 1950

PRESENT :

President

Dr. A. P. Bajpayee, M.B., B.S., P.M.S.

Members

Dr. H. N. Bhatt, F.R.C.S.E.

Major R. N. Bose, M.B.

Dr. V. S. Mangalik, M.D.

Dr. Rameshwar Singh, L.M.S.

Dr. P. S. Verma, L.M.P.

Dr. Chandhri Hardeo Singh Verma, L.M.P.

Dr. Ram Narain Lal, F.S.M.F.

Dr. S. P. Gupta, M.D., B.S.

Dr. S. S. Bose, M.B., B.S.

Registrar

Dr. R. N. Shukla, M.B., B.S.

1. The minutes of the last meeting were confirmed.
2. Government notifications announcing the appointment and election of members were read and recorded.

3. The audit and inspection note on the accounts of the Council for the year 1948-49 was considered and the Registrar's annotations were approved.

4. Resolved that the railway authorities be re-approached to help the Medical Council in taking proceedings against Dr. Damodar Singh, L.S.M.F., by producing full evidence in this particular case. Further resolved that the Legal Remembrancer may as well be addressed to clarify the issue in view of the last communication from the railway.

5. Resolved that necessary changes, as suggested by Government, be made in the seal and its size be reduced. The Registrar to decide the size of the new seal.

6. Letter from the Medical Council of India stating that the proposal for a common design of seal for all Medical Councils has not been accepted was recorded.

7. Resolved that the registration fee be raised to Rs. 20.

8. Resolved that the Government be informed that the presumption made by them in G. O. no. 2443-B/V—1989-47, dated 22nd July, 1949, is correct.

9. Resolved that the name of Dr. Indra Narain Saksena, L.M.F., may now be restored.

10. The Medical Council did not agree with the view of the Medical Council of India that medical practitioners of foreign nationality may be registered if they are attached to medical colleges provided they do not engage in private practice for personal gain, and resolved that such doctors should only be registered when they come within the principle of reciprocity of registration.

11. Resolved that the suggestion of the Medical Council of India that doctors registered in the United Kingdom in the Commonwealth (erstwhile Colonial) and Foreign parts of the British Medical Register should not be registered in terms of reciprocity, be followed.

12. The report of the Standing Committee, which met on 8th May, 1950, was approved with slight modifications.

13. Not considered necessary.

14. Resolved that the rules recently prescribed by the Government regarding the gradation of fees for attendance for the medical officers for whom the fees have been prescribed should be withdrawn forthwith.

15. Resolved that a reminder may again be sent to the Government to expedite the passing of the amendments to the U. P. Medical Act.

16. Not moved.

A. P. BAJPAYEE,
President, Medical Council,
Uttar Pradesh.

R. N. SHUKLA,
Registrar.

BOMBAY MEDICAL UNION

Copy of the Resolution passed at the Special General Meeting of the Bombay Medical Union held on 25th July, 1950, to condole the death of Dr. S. B. Gadgil, B.A., F.R.C.S. (Eng.), who died on 11th July, 1950

Resolved

'That this Special General Meeting of the Bombay Medical Union places on record its deep sense of sorrow at the sad demise of Dr. S. B. Gadgil, B.A.,

F.R.C.S. (Eng.), a member of the Managing Committee and a Past President of the Bombay Medical Union.'

'That in him, the Bombay Medical Union and the profession have lost a very sincere worker, an able surgeon and a great Indian.'

'That a copy of this Resolution be forwarded to his nearest relatives, to the Press and to the Medical Journals.'

LINSEED STRAW TO REPLACE JUTE

(Reproduced from a Release dated 14th June, 1950, issued by Press Information Bureau, Government of India)

As a result of research carried out at the instance of the Indian Central Jute Committee, it has been found that linseed straw, which is at present being burnt away, can replace jute fibre successfully and between 33 and 74 per cent of the fibre can be used for sacking warp. It is estimated that every maund of straw would yield 20 per cent fibre. The availability of linseed fibre is likely to prove a great relief to meet shortage of jute.

GROUNDNUT HUSK AS CATTLE FODDER

(Reproduced from a Release dated 10th June, 1950, issued by Press Information Bureau, Government of India)

The possibility of using groundnut husk, which is at present being wasted, as cattle fodder, particularly during scarcity conditions, is under investigation at the Indian Veterinary Research Station, Izatnagar. The chemical examination of the husk indicated that the crude protein and crude fibre contents are high as compared with wheat chaff (*bhoosa*) and rice straw. Exploratory feeding experiments on cows for about three months showed that the use of groundnut husk had no ill effect on them while in the case of adult bullocks it was found that they actually gained in weight to the extent of 20 per cent. It was also found that groundnut husk mixed with equal proportions of wheat *bhoosa*, small quantity of rape cake and salt was relished by cows, calves, bullocks and buffaloes. Further trials showed that it can be safely fed to adult and dry animals up to 50 per cent of roughage but for longer period feeding, it should be restricted to one-fourth or one-third of roughage only.

MEDICINE SPOONS

(Abstracted from the *Pharmaceutical Journal*, No. 4505, Vol. 164, 4th Series. Vol. 110, 4th March, 1950, p. 173)

A SPECIFICATION has been issued by the British Standards Institution (B.S. 1348 : 1949) for spoons used in measuring medicine. Details are given of the requirements for teaspoons and tablespoons; subject to a tolerance of ± 5 per cent, the levelled capacity of the teaspoon must be 60 minims (1/160th of an Imperial pint) and of the tablespoon, 240 minims (1/40th of an Imperial pint). The spoons are to be made of glass, china, chromium-plated metal or a plastic material.

The spoons are to be shaped in the form of ellipse, the nominal length of the internal rim being 1½ in. for teaspoons and 2 in. for tablespoons, each spoon having a handle sufficiently strong for use with viscous substances such as syrup, without bending the handle, and 3 in. long for teaspoons, or 5 in. for tablespoons. Where the material permits the spoons are to be coloured red. The specification lays down that such

spoons should be marked 'B.S. 1348' and should bear indelibly the word 'medicine'.

INDONESIA LAUNCHES VAST YAWS-CONTROL PROJECT

(Press Release, SEA/PR/50-33, New Delhi, 13th June, 1950, issued by W.H.O. Regional Office for South-East Asia)

A NATION-WIDE programme for the control of yaws and syphilis, recently launched by the Indonesian Government with financial assistance from the United Nations International Children's Emergency Fund (UNICEF) and with technical guidance from the World Health Organization (W.H.O.), is developing satisfactorily according to a report received in New Delhi yesterday from Dr. Kenneth Hill, W.H.O. Expert Consultant attached to the project. Yaws is a disease resembling syphilis but non-sexually transmitted. It affects an estimated 15 per cent of Indonesia's population and is particularly serious among children.

The project, which is under the direction of Dr. Kodijat of the Indonesian Health Services, is planned to provide facilities for penicillin treatment of yaws sufferers among 12 million of the total 80 million of Indonesia's population. It will concentrate on 'infective' cases of the two diseases. In villages near Djakarta where the scheme is already operating penicillin treatment is reported to have produced rapid healing.

Dr. Hill reports that in Jogjakarta a large palace has been taken over as headquarters for the project, and is being converted into offices, a laboratory, and lecture rooms where field staff will be trained. Fifty nurses have already been recruited and are receiving both theoretical instruction and field training. They will work in teams under the direction of qualified doctors.

Four Indonesian doctors are to receive specialized training in modern methods of diagnosis and treatment at the Simla headquarters of the W.H.O. venereal disease control team at present operating in the Himachal Pradesh, North India. Two of them, Dr. Sjamsuddin and Dr. Soebekti, have already arrived in India. On their return to Indonesia all four will be engaged in the yaws-syphilis control project.

Later, it is intended to build a ward of 10 beds at the project's Jogjakarta headquarters for the observation of special yaws cases for research purposes. A research team is being organized, and it is proposed that strains of the organism which causes the disease will be flown to the W.H.O. Reference Laboratory in Baltimore, U.S.A., for intensive study.

BEVAN TO VISIT INDIA AT EARLIEST OPPORTUNITY

RAJKUMARI AMRIT KAUR'S TRIBUTE TO U.K. HEALTH SERVICES

(Reproduced from a Release No. B.F. 731, issued by British Information Services, Mansingh Road, New Delhi)

Speaking at a luncheon at India House, London, on 14th June in honour of Rajkumari Amrit Kaur, Mr. Aneurin Bevan, Britain's Minister of Health, said he wished very much to go to India and see for himself medical administration there in action.

Mr. Bevan felt sorry that it was not possible for him to avail of the opportunity of visiting India early this year. However, he added, he would seize such an opportunity just as soon as he possibly could.

Rajkumari Amrit Kaur said that she was always delighted to visit Britain, a country which had provided her with a great deal of material which was useful to her in her work. She was certain that on every occasion she visited the U.K. she would be able to take back to India useful hints for the betterment of the health service there.

Praising Britain's National Health Service, Rajkumari Amrit Kaur said that if a similar scheme could be instituted in India she was certain that it would be of immense benefit to the nation. She was most anxious that Mr. Bevan should visit India because she felt convinced that he could impart a great deal of useful knowledge to the people in charge of the health service in India by virtue of his unprecedented experience of running the scheme in Britain.

Contributions to W.H.O.

At a press conference held the same day, Rajkumari Amrit Kaur referred to the contributions India had made to the World Health Organization. India had contributed greatly to the W.H.O., she said, by pressing for the division of the world into zones, and the first zonal centre established in India was already in the third year of its work.

Rajkumari Amrit Kaur said she was visiting Egypt on her way back to India at the invitation of the Egyptian Government. She would take the opportunity of studying the headquarters of the W.H.O. in the East Mediterranean Zone at Alexandria. There was a sanitary bureau in this zone and much was being done for T.B. relief for rural patients. In this zone, she said, they had put up huts very cheaply to isolate such patients.

Referring to the nursing services in India, the Rajkumari said that nurses who had come to Britain for training had invariably proved their merit. Paying a further tribute to the British health scheme, she said that India was fortunate to benefit by the experiences of Britain and in particular the personal advice of Mr. Bevan and Dr. Edith Summerskill, Minister of National Insurance. She looked forward to their visiting India in the near future.

Referring to the housing shortage in India, the Health Minister said that a factory for making pre-fabricated houses would be in full production by the end of the year, when on an average 300 houses would be turned out every week. The speed with which these houses could be erected was one of the main reasons for making this experiment.

PROFESSOR W. SCHÜFFNER

(Reproduced from *British Medical Journal*, Saturday, 28th January, 1950, p. 254)

PROFESSOR WILHELM SCHÜFFNER, whose death has just been announced from Holland, was born near Minden, in Hanover, in January 1867. He received his medical education at the Universities of Erlangen, Würzburg, and Munich, and at the age of 30 became chief medical officer to large estates in eastern Sumatra. It was during this period that he first described in 1899 the stippling of the red cells infected with *Plasmodium vivax*, the condition now known throughout the English-speaking world as 'Schüffner's dots'. In 1916 he became medical adviser to the Government of the Dutch East Indies and had much to do with improving health conditions in Java and Sumatra. From 1922 to 1937 he was professor of tropical hygiene at the Royal Colonial Institute in Amsterdam, and from 1924 to 1937 he was medical director of the Institute. From 1937 until 1944 he continued to act as director of the Schüffner Laboratories of the Institute.

Schüffner's contributions to tropical medicine were of outstanding importance. As early as 1900 he had

recognized the value of oil of chenopodium in the treatment of ankylostomiasis. On his return to Holland he became specially interested in leptospirosis, which he had first encountered in the East. He was a world authority on this subject, and first showed the importance of the agglutination test in diagnosis. Many of his communications on this and other subjects were published in English. It was largely as a result of his work and his address to the Royal Society of Tropical Medicine and Hygiene in 1934 that leptospirosis was recognized as a common and important disease of man and animals. Many will look back with pleasure to the kindly, generous man they knew before the Nazi plague spread over Europe. Few of those who attended the International Congress of Tropical Medicine at Amsterdam in September 1938, will soon forget his anguish at the gathering storm which was so soon to overwhelm his own and his adopted country.—G. M. F.

OBITUARIES OF PHYSICIANS IN THE U.S.A. IN 1949

(Abstracted from the *Journal of the American Medical Association*, Vol. 142, No. 3, 21st January, 1950, p. 184)

The obituaries of 3,331 physicians were published in the journal during 1949.

An analysis shows that the average age at death was 67.2 years. The ages of the decedents ranged from 21 to 99 years; the largest number of deaths occurred between 70 and 74.

The results reveal heart disease to be the leading cause of death, with a total of 1,375 deaths, or 41 per cent of all deaths among physicians. Of these, 706 were due to coronary occlusion, embolism and thrombosis, 172 to angina pectoris and other coronary diseases, 273 to diseases of the myocardium and endocardium and 224 to other diseases of the heart. The average age at death from diseases of the heart was 66.8 years.

Diseases of the nervous system caused 432 deaths. Four hundred and five, or 12 per cent of all deaths, were caused by cancer and other malignant tumours; 157 were of the digestive system, 47 of the respiratory system, 74 of the genito-urinary system and 127 of other and unspecified sites. Physicians died at an average age of 68.0 years from cancer.

Accidents caused 138 deaths.

A total of 895 military deaths among physicians has been reported in the journal since the outbreak of World War II; of these, 318 physicians were killed in action and 577 died during military service.

DRUGS RULES, 1945

AMENDMENT TO FORM 21

(Notification No. F.1-19/48-D., Government of India, Ministry of Health, New Delhi, 27th June, 1950)

In exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely:—

In Schedule 'A' to the said rules, in Form 21 under the heading 'Conditions of licence' after condition 3, the following shall be inserted, namely:—

'4. If the licensee wants to sell, stock, exhibit for sale or distribute, during the currency of the licence, additional products specified in Schedule "C" but not included in this licence, he should apply to the

Licensing Authority for the necessary permission. This licence will be deemed to extend to the products in respect of which such permission is given. This permission should be endorsed on the licence by the Licensing Authority.'

(Sd.) J. N. SAKSENA,
Under Secretary.

NOTIFICATION

(No. F.1-5/48-D., Government of India, Ministry of Health, New Delhi, 10th July, 1950)

In exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendments shall be made in the Drugs Rules, 1945, the same having been previously published as required by the said sections, namely:—

I. In the said rules, for Rule 106, the following rule shall be substituted, namely:—

'106. Diseases which a drug may not purport to prevent or cure.

No drug may purport or claim to prevent or to cure one or more of the diseases or ailments specified in Schedule J or to procure or assist to procure miscarriage in women.'

II. For the heading to Schedule J annexed to the said rules, the following heading shall be substituted, namely:—

'Diseases and ailments (by whatever name described) which a drug may not purport to prevent or cure.'

(Sd.) J. N. SAKSENA,
Under Secretary.

INDIAN MEDICAL FORUM

We have received the first two copies of this journal (January and February 1950 issues). They include useful articles of medical interest, viz, medical stock, medical education, B.C.G. vaccination, etc. The format and printing are good. Available from 27, Bentinck Street, Calcutta, at the annual subscription of Rs. 10.

DOMUS CHIRURGICA

(Reproduced from the *Medical Journal of Australia*, Vol. L, 37th Year, No. 12, 25th March, 1950, p. 411)

The International College of Surgeons was created in order to foster the close relationship between surgeons of the world. Through its efforts a section of the *Domus Medica*, at the College headquarters, 1516 Lake Shore Drive, Chicago, will become an international home for surgeons and will be known as *Domus Chirurgica*. It will be under the direction of Dr. Valentin Chavry. It is pointed out in the *World Medical Association Bulletin*, of October 1949, that at *Domus Chirurgica* the surgeon will be able to obtain complete information about conferences, congresses and other professional meetings and also post-graduate courses of instruction. Microfilm reproductions of articles from surgical literature will be obtainable. A travel service will be installed and information on what different countries have to offer will be supplied. It is thought likely that the College will eventually establish offices, similar to that in Chicago, in most of the principal countries of the world. The establishment of *Domus Chirurgica* is an encouraging step in international understanding and in surgical progress.

THE JOURNAL OF BONE AND JOINT SURGERY

(British Volume 32-B, No. 1, February 1950)

We have received a copy of the February 1950 issue of this journal which is also the first number in the new volume 32. It contains many papers of orthopaedic interest—clinical reviews and studies, pathology and basic sciences, atlas of general affections of the skeleton, proceedings and reports, and a bibliography of Abraham Colles (of Colles' fracture fame). The paper and printing are of high quality. The journal is the official publication of orthopaedic surgeons of British Commonwealth and the U.S.A. There are 4 American issues and 4 British issues in a year, obtainable from Messrs. E. and S. Livingstone, Ltd., Teviot Place, Edinburgh, at the annual subscription of £2-10.

THE NOBEL FESTIVAL

(Reproduced from *Jour. Amer. Med. Assoc.*, Vol. 142, No. 5, 4th February, 1950, p. 355)

THE annual Nobel festival on the anniversary of the death of Alfred Nobel, 10th December, is one of the most brilliant festivals of Swedish literary and scientific life. As has been done for many years, it was held in the Concert House in Stockholm in the presence of members of the royal family, the diplomatic corps and a large number of Swedish officials and scientists. Three prize-winners were present: Hideki Yukawa (physics), William Francis Glauque (chemistry) and Walter Rudolf Hess (medicine). The Nobel prize in medicine of this year was divided between Hess and Antonio Egaz Moniz, but Dr. Moniz was unable to attend. He received his prize later through the Swedish minister in Lisbon, Portugal. The winners were introduced to the audience with short speeches from members of the societies charged with the distribution of the prizes. At the end of each introductory speech, the winner was asked to step down from the podium to receive the prize (a cheque and a diploma) from the hands of Crown Prince Gustaf Adolf. The medical prize-winners were addressed by Dr. Herbert Olivecrona, professor of neurosurgery in Stockholm.

After the festival in the Concert House the Nobel Banquet was held in the Golden Hall of the Stockholm City Hall. On 12th December the prize-winners attended a dinner given by King Gustav in the royal castle.

CONTROL OF SYPHILIS

MODERN TREATMENT AND DIAGNOSIS METHODS
INTRODUCED

(Press Release, SEA/PR/50-22, dated 24th April, 1950)

A PILOT campaign for the rapid control of syphilis in a rural community, initiated last December as a joint undertaking of the World Health Organization and the Himachal Pradesh Government (India), has now entered into its final phase according to Dr. N. Jungalwalla, Adviser on Venereal Diseases to the W.H.O. Regional Office for S.-E. Asia. Using the most modern methods of mass-diagnosis and treatment, this pilot campaign, which Dr. Jungalwalla states to be the first of its kind in any S.-E. Asian country, is intended to establish a sound basis for launching further vitally important control operations in other areas throughout S.-E. Asia where similar disease problems exist.

The W.H.O. venereal disease control team, which for the last nine months has been training doctors and laboratory workers from all over S.-E. Asia at its Simla headquarters, selected the Ghund area, about 30 miles east of Simla, for the pilot project, because a high proportion of the inhabitants of this hill region were

believed to be infected, and because its comparatively isolated situation made it suitable for obtaining reliable information on the results of the mass-treatment planned.

Last December the W.H.O. team together with helpers from the Himachal Pradesh health services spent two weeks in the Ghund area examining practically the total population of 1,900 persons, and taking about 1,500 blood samples for laboratory testing. A case card was made out for each person tested, and each was given a first injection of a special penicillin compound (300,000 units of procaine penicillin G with 2 per cent aluminum monostearate). Laboratory tests of the blood samples taken revealed that about 70 per cent of the adult population were suffering from the disease.

The second and final stage of the campaign which is now in progress is stated to have two principal aims: (a) to give further penicillin treatment to persons who still need it; and (b) to obtain further blood samples from the population in order that exact statistics may be compiled showing the efficacy of the first mass-treatment given in December. The total population is therefore being invited to attend either at Bagain, in the Giri valley, or at Ghund Durbar on the adjacent hill-top. In order that the people may see for themselves why they are asked to contribute their blood a second time, the blood tests are being carried out in a field laboratory set up in Ghund Durbar itself under the supervision of Dr. J. Kvittingen, W.H.O. laboratory expert. All the necessary supplies and material are carried to the site by mules, while the team members journey on foot up and down the steep mountain sides.

Dr. J. C. Cutler, leader of the W.H.O. team expresses himself as satisfied with the results obtained to date. 'It is significant', he states, 'that since the beginning of the campaign in December, not a single new case of early syphilis from the Ghund area has been reported to the local dispensary. Previously from twenty to twenty-five cases occurred each month.' Dr. Cutler believes that a high proportion of cases have responded to the first treatment of one single injection of penicillin given last December.

The Ghund operation is being followed with close attention by health authorities in most countries of S.-E. Asia who believe that it will open a new era in the treatment of venereal disease in this part of the world. Before the introduction of penicillin therapy a patient was required to take a treatment each week over a period of 18 months at comparatively great cost. Now the period necessary for actual treatment has been reduced to two weeks or less, and the cost comes out at about Rs. 4 per patient. Parallel with this advance in treatment methods, more rapid and less expensive techniques for carrying out laboratory blood tests have been developed. These are now being taught at the Simla laboratory of the W.H.O. team.

Dr. Cutler reports that a number of other districts in the Himachal Pradesh have requested his team to undertake mass-control operations on the lines of the Ghund campaign. The team has agreed to go to Balsan next week for this purpose. Arrangements are also being made with the Himachal Pradesh Government for similar operations to be undertaken in other districts by Indian doctors and laboratory workers who have completed their training with the W.H.O. team. W.H.O. is able to supply a certain quantity of penicillin and essential laboratory equipment for these projects. Already rural dispensaries at Chamba, Mandi and Nahan have the necessary personnel and equipment to carry out both diagnosis and treatment on modern lines.

Dr. Jungalwalla, of the W.H.O. Regional Office for S.-E. Asia, accompanied the W.H.O. team on its journey to the campaign area last week, while Mr. E. P. Moon, Chief Commissioner of Himachal Pradesh, and Dr. Ghirdari Lal, Medical Officer in charge of the

district, also visited Bagnin and urged the local people to co-operate whole-heartedly in this campaign which, by bringing under control a disease that had undermined their health for decades, held out to them a promise of improved economic well-being as well as greater health and happiness.

\$52,320 (RS. 2½ LAKHS) GRANTED BY W.H.O. FOR MEDICAL SUPPLIES TO S.-E. ASIAN COUNTRIES

(Press Release, SEA/PR/50-36, dated 17th June, 1950)

MORE than half of the world total of \$100,000 granted by W.H.O. in 1950 to aid Member States in procuring essential medical supplies has been allocated by the W.H.O. Executive Board to three South-East Asian countries, announced Dr. C. Mani, Regional Director of W.H.O. for S.-E. Asia on his return to New Delhi on Saturday. Dr. Mani together with Dr. R. L. Tuli, Regional Planning and Operations Officer of W.H.O., has spent the last six weeks in Geneva attending meetings of the Third World Health Assembly during May and of the W.H.O. Executive Board which concluded its sixth session last week.

The three South-East Asian countries which between them share an allocation of \$52,320 (Rs. 2,49,000) are India, which receives \$25,000 (Rs. 1,19,000), Thailand, whose allocation is \$16,320 (Baht 359,000), and Afghanistan (11,000 dollars). The Executive Board recommended that these sums should all be employed for the purchase of D.D.T. and other supplies for malaria control operations in the three countries. Some reimbursement for the cost of these supplies in local currencies will be expected.

The remainder of the hundred thousand dollar total, stated Dr. Mani, is divided between Ethiopia (\$5,500), The Hashemite Kingdom of the Jordan (\$9,600), Portugal (\$4,500), Yugoslavia (\$10,080), Finland (\$12,000) and Monaco (\$6,000) and is to be used for purposes varying between x-ray apparatus and sulphone drugs for leprosy treatment.

Dr. Mani explained that the Executive Board were insistent that W.H.O. was not primarily a procurement agency, and could grant supplies only according to established criteria. The criteria adopted by the Board were: (i) The importance of the programme to the country receiving aid, and its relationship to W.H.O. priorities and programmes, and (ii) a guarantee of the country concerned to carry on the programme and utilize the supplies in a correct way for the execution of the programme.

The total of \$100,000, according to Dr. Mani, represented a sum allocated by the Second World Health Assembly for supplies in 1950. No provision for supplies had been made in the 1951 Budget recently adopted by the Third World Health Assembly.

Another important decision of the Executive Board, Dr. Mani revealed, was to establish an expenditure ceiling of \$6,150,000 for 1951. The original budget appropriated by the Third World Health Assembly last month amounted to \$7,300,000. The million dollar cut was considered necessary because the income which can reasonably be expected to be received in respect of 1951 will be substantially less than the budget appropriated, several States being still in arrears with their contributions to the 1948 or 1949 budgets, or both. Seventy-five Member and Associate Member States have been assessed for the 1951 regular budget, including the nine countries which have declared they no longer consider themselves as members of the Organization. Similar action had been taken by the W.H.O. Executive Board at an earlier session with regard to the 1950 budget of \$7,500,000, which was cut down to \$6,300,000 for the same reason.

A large-scale scheme for the training in India of child health workers from South-East Asian countries

had received unanimous and whole-hearted support from the Joint W.H.O./UNICEF Committee on Health Policy, whose recent meeting in Geneva was also attended by Dr. Mani and Dr. Tuli. This training project, which will be financed partly by the Indian Government and partly by the United Nations Children's Emergency Fund (UNICEF), will be carried out in the All-India Institute of Hygiene and Public Health in Calcutta, under the direction of Dr. C. ... will group students from several ... Asia. W.H.O. will be technical adviser to this project. Apart from formal courses, the students will receive instruction in rural and urban centres and will be trained in aspects of maternal and child health work, including nursing. The cost of this six-year project is estimated at \$1,860,000. W.H.O., according to the established policy of the two agencies, will carry the technical functions in this programme.

QUARANTINE RESTRICTIONS

(Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta, Director-General of Health Services, New Delhi, 27th July, 1950)

INFORMATION has been received by the Director-General of Health Services that the health authorities of Mauritius have declared India infected with cholera by air route.

In order to avoid delay and inconvenience on entry into Mauritius, passengers leaving India by air are required to produce international certificates of inoculation against cholera, showing that inoculation has been performed not less than seven days and not more than six months prior to arrival in Mauritius.

NITROGEN MUSTARD HYDROCHLORIDE

We understand small stocks of nitrogen mustard hydrochloride (for the treatment of Hodgkin's Disease and Leukæmias) are now available with Messrs. Bools Pure Drug Co. (India), Ltd., Bombay. Doctors and hospitals requiring this drug should apply to the Drugs Controller, India, Directorate-General of Health Services, New Delhi.

RE.: THE UTRECHT FAIR, 1950

You are probably aware that in the Netherlands is held twice every year at Utrecht the Royal Netherlands Industries Fair (International)—the Spring Fair in March/April and the Autumn Fair in September.

The ever-increasing number of foreign articles exhibited at the Royal Netherlands Industries Fair (International) at Utrecht, which, since 1947, surpasses by far the number of the home products, shows clearly enough the outstanding international character of this Fair and that it is not aimed at this Fair to promote the export of Dutch goods only.

This Fair exhibits a vast array of products from every country competing in the world market. Arranged in sections according to their products, a large number of industries are represented in the Fair, a visit to which therefore, provides a unique opportunity of obtaining a fairly general review of each industry not only of the Netherlands but also of practically every country engaged in the world export trade.

The Autumn Fair of this year is due to be staged from the 5th to 14th September, 1950. As already stated the Fair is arranged in sections among which

there is a special section exclusively devoted for the display of Medical and Surgical Instruments and Nursing and Hospital Equipments. This aspect of the exhibition will I am sure be of particular interest to the medical world.

In the ensuing Autumn Fair this section will occupy double the area compared with the space taken up at the Spring Fair in last March and there will be a comprehensive display of a very large assortment of medical instruments and apparatus and hospital equipments. There will also be exhibited various latest and important medicinal preparations and surgical appliances manufactured not only in the Netherlands but also in various foreign countries.

The foregoing information is passed on to you in the hope that the same will be of special interest to the medical profession and trade in this country.

A. C. H. GRAAFLAND,
for Commercial Counsellor.

ROYAL NETHERLANDS EMBASSY,
298, BAZARGATE STREET,
BOMBAY.

The Indian Medical Gazette

Fifty Years Ago

OUR SPECIAL NUMBER

(From the *Indian Medical Gazette*, August 1900,
Vol. 35, p. 321)

THE present number of the *Indian Medical Gazette* is a special one, entirely devoted to questions connected with stone in the bladder and the various operations for the relief thereof. The fact that stone in the bladder is a very common disease in many parts of India is well known, but when we attempt to consider the causation of that prevalence we are met with many difficulties. The question is unsettled in India as it is in England. We can no more say with certainty why stone is so common in the Punjab and Sindh than we can say why it is common in Norfolk and almost unknown in Ireland. The question is a difficult one and intimately depends upon considerations of physiological chemistry as yet imperfectly understood. One fact is certain that no rough and ready theory will explain the whole case; there is a multiplication of factors. Lime in the drinking water and concentrated state of the urine in the hot weather is a theory which has been put forward by Major J. A. Cunningham, I.M.S., but though we may admit both these as factors, we cannot believe they are the whole of the matter. We believe there are rivers and water-supplies in parts of Madras where we never get stone cases that have as much lime in them as any river in the Punjab or Sindh; nor perhaps is it safe to assume that the chemistry of the body is so simple as to take in lime in the drinking

water and pass it into the bladder as a stone. No lime, no calculi say some; possibly so, but yet there is lime where there are no calculi. The other theory, which judging from the remarks of our correspondents is the one which commends itself to the majority, is the dietetic theory first sketched out as regards India by Major A. E. Roberts, I.M.S., in his paper in the Transactions of the first Indian Medical Congress. This theory, which its author still claims to be no more than a broadly stated hypothesis, is that if we look at the distribution of calculus disease in India we are at once met with the fact that in the rice-eating districts of India, Bengal, Assam, Madras, etc., stone is certainly rare, whereas in the wheat-eating districts of the North-West Provinces, Punjab and Sindh, stone is much more common. So much can be stated with certainty, but to go further than this is here impossible. That the staple food of the people has some relation to the prevalence of stone must be admitted, but more than this we cannot say. The amount of salt used by natives of various provinces is possibly another factor, but what extent a small consumption of salt affects the incidence of stone has not yet been worked out. Many considerations point to the co-extensive prevalence of cataract and stone. We must, however, leave this part of the subject and confess that little or nothing is certainly known as to the causation of stone in certain countries, districts and provinces.

To turn to our papers—the one fact that clearly emerges from a perusal of the various papers and opinions that we have here collected together is the extraordinary safety and extraordinary popularity of the operation of litholapaxy, which surgeons in India, rapidly grasping the grand idea of Bigelow, have permanently established as the best and safest operation in all ordinary cases. The statistics given in our various articles and especially those given by Captain H. Smith, I.M.S., show this clearly. We know of no collection of statistics on the operation which so clearly points out the relative safety of litholapaxy and lithotomy in regard to the ages of the patients—a point long ago emphasized by Sir Henry Thompson.

Another point brought out by these articles is the desire on the part of surgeons for the further extension of crushing as opposed to the cutting operations—Keith's perineal lithotomy, the use of the giant lithotrite both point to the popularity of the crushing operation. Lithotomy, however, is not without its advocates, though it is clear that in many cases the surgeon uses it from necessity rather than choice. Nor must the present-day statistics for lithotomy be taken as the best that that operation could produce. By the majority of surgeons lithotomy is only done when for certain reasons litholapaxy is not applicable, therefore the cases for lithotomy are thus selected in a way which does not make for high-class statistical success. To

some extent the same remarks apply to the suprapubic operation. A Russian surgeon publishes 102 suprapubic operations with only two deaths. These, as far as we know, represent the total of his operations, that is, he operated on all cases by this method, hence his success; but in India the suprapubic operation never was popular; it was always reserved for cases of difficulty, hence its high percentage of mortality. There is another important point to be considered before we conclude—that is, the very unequal equipment of different hospitals in the matter of lithotrites. A glance at the replies to our circular will show that many surgeons do lithotomy rather than litholapaxy, as we said above, from necessity rather than choice. Most hospitals have their time-honoured case of lithotomy instruments, but only a few have complete sets of lithotrites. To be able to meet every case of stone by the operation of litholapaxy the experienced surgeon should have the following lithotrites 5, 6, 8, 10, 12, 14 and 16 (Weiss), for a well-equipped hospital we would add a no. 4, 20 and a 'giant' lithotrite. To provide these with canulas, aspirators, etc., considerably over £60 is necessary, and we cannot but admit that every municipal dispensary cannot afford so much for one class of operation, but they could be got gradually, and the stock kept up in good repair. We commend the remarks on this subject by Dr. Keegan in the above article to the attention of Administrative Medical Officers and to the Local Governments.

Historical sketch of stone in India

'We must see for ourselves what is to be the future operation for the vast majority of calculi we meet with in India. Our opportunities for treating stone are simply unrivalled, and we need not look to England or indeed to any country in Europe for guidance'.

D. F. KEEGAN,
(I.M.G., p. 42, of 1889).

Current Topics, Etc.

Clinical Evaluation of Various Tests for Occult Blood in the Fæces

By S. O. HOERR *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 24th December, 1949, p. 1213)

THE results of a series of tests for occult blood in the stools of 140 unselected hospital patients, none of whom was given a special diet for the tests, are recorded. These patients had a wide variety of diseases.

Benzidine and orthotolidine are too sensitive to be useful reagents for routine testing of stools from

patients who have not been prepared with a meat-free diet.

The guaiac test is not too sensitive for use on stools from unprepared patients eating their usual food.

The guaiac test is valid when performed on faeces smeared directly on to filter paper; it may be used on faeces from a rectal glove.

The guaiac test is suitable for office use, requiring only three easily obtainable reagents which retain their stability for at least one month.

In a positive guaiac reaction there must be a definite change to blue or dark-green within thirty seconds after the hydrogen peroxide is added.

Positive guaiac reactions denote significant organic bleeding in a high proportion of cases.

Negative guaiac reactions do not rule out the existence of organic disease of the gastro-intestinal tract including malignant growth.

Because of the simplicity of the guaiac test and relative clinical accuracy of a positive reaction, routine use of the test on a par with the blood cell count and urinalysis is recommended.

Melena : A Study of Underlying Causes

By H. L. THOMPSON

and

D. W. MCGUFFIN

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 24th December, 1949, p. 1205)

THE present report is based on 293 cases of gastro-intestinal bleeding in which melena was a prominent clinical sign. The study has been made from the points of view of (1) the site of origin of the bleeding and (2) the underlying pathologic condition. Anatomically, the sources of hæmorrhage included all portions of the gastro-intestinal tract from the œsophagus to the rectum, inclusive. The anus, where bleeding from internal hæmorrhoids commonly originates, was not included in this study for obvious reasons. The degree of melena was marked (grade 4) in all groups except that of bacillary dysentery.

In the largest single group of cases peptic ulcer was the pathologic condition from which melena originated. Bacillary dysentery was second in frequency as a cause of melena. The next largest number, exclusive of bacillary dysentery, was comprised of diseases of the colon and rectum. Otherwise, with respect to the anatomic origin of hæmorrhage the cases were fairly evenly distributed between the œsophagus, stomach and colon with a relatively small number, exclusive of peptic ulcer, originating in the small intestine. There is a miscellaneous group in this as in nearly every series reported in the literature. In this instance it is unusual, in that it contained the remarkably small number of 3 cases.

There were 87 cases of peptic ulcer, representing 29.6 per cent of the series. In the present group there was the unusual predominance of duodenal ulcer in white males. It is worthy of note that 55 per cent of cases occurred in the fourth through the sixth decades, a factor of importance when correlated with mortality. In light of the concepts of Finsterer, Gordon-Taylor, Heuer and Allen, gastro-intestinal hæmorrhage 'is a much more serious condition in patients over 45 years of age. Under certain conditions surgical treatment should be employed in cases within this age group. Although it was employed as a method of therapy in a relatively small proportion in this series, it is of some interest that there was a lower mortality of 20 per cent for surgical treatment as against 24.9 per cent when non-surgical treatment was employed. The fact that

the proportion of surgically treated patients in the present group is small no doubt is responsible for mortality as low as 20 per cent. It will be interesting to ascertain the mortality resulting from the programme of surgical treatment of peptic ulcer complicated by hæmorrhage now under way at this hospital.

There was associated hæmatemesis in 79.5 per cent of cases of peptic ulcer. We have shown previously that the mortality in peptic ulcer complicated by hæmatemesis ranges from 20 to 36 per cent. It is noteworthy that gastroscopic confirmation was employed in so small a proportion as 1.1 per cent of cases.

There were 27 cases, 9 per cent, in which œsophageal varices were complicated by melena. Certain similarities with respect to ætiologic factors and clinical features in the groups of peptic ulcer and œsophageal varices have been brought out in the text. Diagnostic confirmation, however, was more difficult to obtain in œsophageal varices, particularly during the stage of active bleeding. The highest death rate in the non-malignant conditions occurred in cases of œsophageal varices. It reached the significant proportion of 70.5 per cent. This figure indicates the urgent nature of gastro-intestinal bleeding from this source. The highest mortality rates in this study of melena occurred in cases of carcinoma. As an important cause of bleeding, carcinoma of the stomach is significant not so much from the standpoint of incidence (23 cases) as from the extremely high mortality of 90 per cent, which resulted from bleeding in the non-surgically treated cases. Likewise, it is important to note that 78.5 per cent of cases occurred between the sixth and eighth decades of life, a factor of apparent significance for the same reason that bleeding from peptic ulcer is more important in the older ages. Of the 13 cases in which surgical exploration of the stomach was performed, the lesion was found to be nonresectable in 10. In the group where nothing more than exploration and/or palliative procedures were performed, the mortality reached the discouraging high of 60.0 per cent. Gross mortality in carcinoma of the stomach associated with melena in this series reached 69.5 per cent.

Of the miscellaneous sources of hæmorrhage from the stomach, hiatus hernia heads the list with 5 cases, or 1.7 per cent of the series.

The most remarkable feature with reference to conditions of the small intestine is the small number of cases. Exclusive of peptic ulcer there were only 6 cases in the entire group, representing 1.4 per cent of the series.

Of conditions localized in the large intestine, the largest number, 63 (21.4 per cent), was comprised of cases of bacillary dysentery. Significantly, 73 per cent of cases occurred within the first decade. Another important fact is that laboratory confirmation with classification of the offending organism was obtained in 100 per cent of cases. The grade of melena was relatively small (2). Mortality was low (2 cases).

The 18 cases of carcinoma of the rectosigmoid comprised 6.1 per cent of the group. The incidence was slightly higher in males, and 67 per cent of cases occurred in the seventh and eighth decades. Hæmatemesis was reported with melena in 2 cases. Important mortality occurred in carcinoma of this region. In cases in which surgical treatment was employed, the mortality was 62.0 per cent as contrasted with 90 per cent in the group wherein non-surgical treatment was utilized. There is no doubt but that non-surgical treatment was applied in the latter group because of the advanced stage of the disease.

There were 16 cases of idiopathic ulcerative colitis, or 5 per cent of the series. Most of the patients were white males, and one-half of the patients were in the third decade of life. Diagnostic confirmation was obtained in all but 18.7 per cent of cases. Surgical treatment was applied in only 2 cases, 12.5 per cent, without mortality; medical treatment was given in

14 cases with the high mortality in this condition of 35.6 per cent.

The total number of cases of diverticulitis of the colon was 11, or 3.8 per cent of the group. This is the only condition in this study in which the occurrence predominated in females (63.6 per cent). There was associated hæmatemesis in 1 case. All portions of the colon were affected, with 63.6 per cent occurring in the descending colon and sigmoid. Non-surgical treatment was carried out in all cases without mortality.

In the group of miscellaneous conditions of the colon, there was 1 case each of carcinoma of the pancreas and prostate with metastasis to the colon and 1 case of splenomegaly.

It is fully appreciated that in many groups in this study the number of cases is too small for accurate statistical evaluation.

Relation of Relapses in Typhoid to Duration of Chloramphenicol Therapy

(From the *Journal of Tropical Medicine and Hygiene*, Vol. 53, January 1950, p. 21)

DURING the past year much information has accumulated on the use of chloramphenicol (chloromycetin) in the treatment of typhoid. All of this confirms the original report of Woodward and others, covering the observations on 10 patients, which clearly indicated that the new antibiotic was of great value in this disease. Continued experience reveals that fever disappears by lysis during the first three or four days of treatment.

These early observations, as well as those of McDermot and his associates, brought out that relapses of typhoid were common in treated patients. In order to eliminate such occurrences, the course of treatment in infected persons has been prolonged. Analysis of the results obtained in 44 patients with typhoid who received chloramphenicol therapeutically has indicated a striking relation between the duration of chemotherapy and the incidence of relapses.

The results warrant the following conclusions. Chloramphenicol (chloromycetin) should be administered in adequate amounts for more than eight days to patients acutely ill with typhoid if relapses of the diseases are to be avoided. There appears to be little advantage in continuing treatment for more than fourteen days.

Experimental Work with the Sulphone Group in Leprosy

(From the *Journal of Tropical Medicine and Hygiene*, Vol. 53, January 1950, p. 16)

IN view of the importance of the paper by Dr. R. G. Cochrane and his colleagues in Southern India we feel justified in giving the following lengthy abstract:

It is clear that whatever sulphone is used, be it diasone and sulphetrone by mouth, be it diamino-diphenyl-sulphone in suspension, or sulphetrone in aqueous solution or in suspension, there is uniform clinical improvement in all cases. Sulphetrone as compared to diasone is apparently more rapid in its action. Four out of the 9 cases on sulphetrone in an average period of eighteen months have become negative, while out of 25 cases with diasone treatment only 4 have become negative. It is interesting to note, however, that all these 4 are children who have received adult doses. While only one of the sulphetrone cases on treatment for more than nine months has deteriorated or remained bacteriologically

stationary, seven cases on diasone have shown no improvement bacteriologically and two no improvement clinically.

With reference to the comparison of diasone and sulphetrone orally with diamino-diphenyl-sulphone and sulphetrone by parenteral administration, it is obvious that the dosage required orally is very much greater (ten to twenty times) than by injection.

The evidence accumulated over the past two and a half years confirms the fact that the sulphone remedies are effective in lepromatous leprosy. The statement made by one of the writers (R. G. C.) at the International Conference at Havana (1948) that the early lepromatous cases under hydriocarpus medication respond as quickly as those under sulphone therapy is confirmed. It will be noted that cases with a bacteriological index of two and under have on an average taken between twenty and twenty-four months to become negative. This compares favourably even with the drug which has the most rapid effect, diamino-diphenyl-sulphone. The average period which this drug has taken to produce a negative result is sixteen months. There are, however, two drawbacks to hydriocarpus therapy when adequately applied. The first is the painfulness of intradermal injections. The second is that while a large number respond to hydriocarpus therapy in the early stages of lepromatous leprosy, more than 50 per cent do not recover within the above period. We believe, however, that the percentage of negatives ultimately with the sulphone preparations would be very much higher. This, therefore, is a point in favour of using the sulphone therapy in all lepromatous cases. When, however, a careful analysis of cases is taken, the high dosage of diasone and sulphetrone (an average of 1,900 tablets in the case of diasone and 6,000 tablets in the case of sulphetrone), as compared with approximately 90 grammes of sulphone by injection, indicates that other things being equal injection of sulphone remedies is the method of choice. It is obvious that twice-weekly injections would be much more convenient and much more economical than large dosages by mouth. On these premises alone, therefore, the method of choice should be sulphone by injection. In considering this question, two other factors have to be taken into account—namely, the toxicity of the remedy and the blood concentration of the drug. With reference to toxicity, this will be considered under the separate derivatives:

(1) *Diasone*.—We have had no signs of immediate intolerance as have been described by other workers—for instance, nausea, vomiting or hæmaturia—but a few cases have shown some deterioration in the blood picture. This has usually righted itself without yeast and iron therapy. There is a general tendency (this observation has been noted by other workers) for the blood picture to improve after six months or so under diasone treatment. As has been pointed out by one of the writers (R. G. C.), diasone tends to produce lepra reaction in a certain number of cases, approximately 30 per cent. In our earlier cases, not here reported, two cases had to stop the drug owing to the severity of the reaction. It was interesting to note that the liability to reaction continues until some 700–1,000 tablets have been taken, after which the likelihood of reaction is very much less, for the proportion of cases showing severe reaction after 1,000 tablets is very small.

(2) *Sulphetrone*.—In the case of sulphetrone the toxic signs were limited to three main ones: (a) anaemia, (b) severe occipital headache, (c) cyanosis. As has been pointed out by previous workers, the cyanosis produced by sulphetrone is of no practical consequence although one of our cases developed a plum coloured complexion. This disappeared on continuance of the drug. Another sign of intolerance of the drug is a very severe occipital headache. It is unassociated with high blood levels and disappears on withholding the drug. There seems to be a somewhat greater

tendency for anaemia to develop with sulphetrone than with diasone, but this readily recovers if the drug is withheld and iron and yeast are administered in adequate dosages. We have always taken care that patients on sulphetrone do not become constipated, for it is believed that constipation tends to produce increased blood concentration owing to the fact that the drug is accumulating in the gut and is retained if the bowels are not kept open.

(3) *Diamino-diphenyl-sulphone*.—We have accumulated clinical evidence that diamino-diphenyl-sulphone in a 25 per cent suspension of groundnut oil is probably the most potent anti-leprosy remedy we have. In several instances there has been an improvement of the bacteriological index, and in some cases this has been quite striking. We, however, have found that apart from the reactions which are produced, when the remedy is continuously administered there are certain toxic signs, some of which are serious. These toxic signs are: (a) anaemia, (b) giddiness, nausea, vomiting, (c) signs of peripheral neuritis as evidenced by pain, particularly along the larger nerve trunks—ulnar and peroneal—and associated with painful limbs and muscles. While sulphone remedies have been stated to have a dangerous toxic effect on nerves, particularly the optic nerve producing optic atrophy, we have had no evidence of permanent damage either to the peripheral nerves or to the special nerve endings such as those going to the retina. The anaemia which is produced on administration of sulphone is sometimes very alarming. In one case the blood dropped to 2.2 millions with a hæmoglobin of 6 grammes, but with the discontinuance of sulphone and the administration of iron and yeast within fourteen to twenty-one days the blood picture had returned to almost normal. One serious symptom is the tendency of this drug to produce signs of liver toxicity. These are nausea, vomiting, hepatic pain and jaundice. All our cases have recovered but we have had no means of assessing the amount of liver damage. Until a dosage is devised which can be guaranteed not to produce these toxic signs it is impossible to contemplate the administration of diamino-diphenyl-sulphone on a large scale. It is of interest to note that Molesworth has stated that a smaller dosage, even as small as 1 gramme per week, appears to be effective in lepromatous leprosy. It is to be remembered that the florid type of leproma responds more dramatically than the slowly progressive lesion, which seems to take a longer time to effect the same clinical improvement. An excellent illustration of this fact is seen in cases from Dr. Kate Young's institution who have shown dramatic bacteriological improvement and all these cases belong to the Mongolian racial group. It may be, therefore, that a dosage of 1 gramme or 15 grammes per week is sufficient to maintain blood levels for effective therapeutic results. In this connection it might be stated that one series of cases had sulphone administered to them by means of a collapsible tube. This method of injection was suggested by a visit the senior author made to the laboratories at Wilmslow where it was used in mastitis of cows. Instead of a cannula, the collapsible tube is fitted with a needle which is screwed on after breaking the cellophane covering. The needle is inserted into the subcutaneous tissues and the suspension slowly 'milked' into the tissues. The collapsible tube can be charged with the dosage required, which would normally be about 1 gramme. If the toxicity of diamino-diphenyl-sulphone can be overcome, this method of injection will be of great value, for instead of having to sterilize all the component parts of a syringe, the only parts that need sterilization are the adapter and the needle.

We believe that diamino-diphenyl-sulphone can be administered provided a dosage of not more than 15 grammes per week is used and that a month's rest is given every two to three months. Further the blood concentration should not be allowed to rise above 2 mg. per cent.

(4) *Sulphetrone (by injection)*.—Sulphetrone has been given by us parenterally in the form of a 50 per cent aqueous solution and a 25 per cent emulsion. We have commenced injections of 25 per cent aqueous solution. These drugs are effective in comparatively small doses, namely 14 ml. (7 ml. twice a week). We are hoping, however, to be able to reduce the dosage as in the case of diamino-diphenyl-sulphone. In the case of sulphetrone we believe that much smaller dosages are effective.

GENERAL OBSERVATIONS

(a) *Tissue concentration*.—It seems to be anomalous that a dose of approximately 4.7 grammes of sulphetrone and 1.2 grammes of sulphone a week is as effective as 6 grammes of sulphetrone by mouth per day. The reason for this effectiveness we believe is due to the ability of the tissues to fix the drug. In experimental sulphone therapy on animals we have found appreciable quantities of sulphone in all the organs of the body—the spleen, the liver, the kidney, the bone marrow—and, therefore, if there is an affinity of the tissues for sulphone and sulphetrone it appears reasonable to assume that injections parenterally will be effective. In connection with the estimation of diamino-diphenyl-sulphone and sulphetrone in the skin, the earlier work showed that we were in error in our conclusion owing to the fact that the anaesthetic that we used produced a colour reaction and therefore made our reading inaccurate and very varied. On the introduction of cocaine, suggested by the I. C. I. Laboratories, the fallacy of a colour reaction produced by the anaesthetic has been overcome and our work on skin concentrations is being repeated. The following conclusions seem reasonable to draw: (i) the sulphones—using this word in the generic sense—are effective in lepromatous leprosy; (ii) parenteral administration is more economical and cheaper than oral administration; (iii) parenteral administration of sulphetrone gives rise to no deterioration in the blood picture; (iv) until a safer dosage of diamino-diphenyl-sulphone is worked out we believe that it is reasonable to recommend for the routine treatment of leprosy, particularly for those cases which do not respond to hydnocarpus treatment or which have relapsed, subcutaneous injections of 50 per cent sulphetrone in water in a dosage of 7 ml. twice a week.

(b) *Morphological changes in the M. lepræ*.—The general observation is that under sulphone therapy the bacilli undergo certain morphological changes. The bacilli first become beaded and then granular forms appear. Ultimately, the majority of bacilli in a slide are mostly granular, even though there is very little difference in the bacillary content of the slide. For instance, in the five illustrations given, six months had elapsed between treatment, and while there was marked clinical improvement the bacteriological index remained the same. Later, the bacilli began to diminish in numbers and ultimately only acid-fast dust was seen. It is impossible as yet to conclude that the fragmentation of the bacilli means death for this fragmentation, although not so marked, is seen with hydnocarpus treatment and probably the fragmented and granular forms indicate that the conditions under which the bacilli are living are unfavourable. Further proof that the fragmented and granular forms may not be dead bacilli has come to us recently. Case no. 30, which over a period of almost two years, showed a steady clinical and bacteriological improvement up to October 1948 (the bacteriological index was reduced from four in November 1946 to two in October 1948) with very little warning, suddenly began to show increased symptoms and fresh subcutaneous nodules appeared, chiefly on the outer extremities of the arms. Smear examination showed that the bacteriological index had increased to three and there had been obvious increase in the bacillary content and there were several globi in fields examined, all the bacilli being granular. It remains for time to show whether there

will be a further increase or whether these bacilli will be dealt with and the case ultimately become negative.

(c) *Reactions and the discontinuance of sulphone therapy*.—Another matter which deserves discussion is the question of rest periods. Because we assume that the sulphones—using this term in the generic sense—are chemotherapeutic agents, we believe that rest periods should only be permitted when there are definite signs of intolerance. For diasone this is shown in the form of a secondary anaemia. With diamino-diphenyl-sulphone suspension, anaemia is likely to occur and toxic symptoms which have already been described, would indicate withholding the drug. For sulphetrone, the only two symptoms which need to be noted are: (i) anaemia and (ii) persistent occipital headache. We are of the opinion that every case probably passes through a stage when there is some exacerbation of the disease, either shown by slight lepra reaction or temporary increase of the bacteriological index or in more severe lepra reaction sometimes of the nature of erythema nodosum leprosum recently described by Woolcott, Johansen and others. The latter condition is a very interesting one which in our opinion is simply one of acute lepra reaction. Sometimes it is so severe that the temperature rises to 104, 105 and even 106°F. and under these conditions the remedy has, of course, to be stopped. We believe, however, that unless the fever is very high, continuance of the sulphone remedies is indicated. In this connection it may be noted that one of the signs of reaction which is relatively frequent is that of iritis. Sometimes this is very severe and the vision may be reduced to almost nil. While the symptom can be extremely alarming, we believe that general principles should be followed and that the drug should be continued. At the same time active measures should be taken to combat the iritis and to dilate the pupil. It is remarkable how a very severe iritis will recover under sulphone therapy with practically no deterioration of vision. We have already mentioned that there is evidence that cases under diasone therapy tend to react during the early stages and after they have been given over 1,000 tablets reaction tends to be either very much less severe or cease altogether. We believe that this reaction phase cannot be avoided and there is no point in stopping the drug or reducing the dose because as the dose increases and the blood concentration either rises to its former level or the drug acts for a more prolonged time, the patient will pass out of the reaction phase.

(d) *Absorption of the drug*.—While it seems preferable that the drug should be exhibited in an oily medium, there have been certain disadvantages particularly in connection with the injection of emulsions of sulphetrone in oil. This has been evidenced in a large number of cases (25 per cent) which have shown areas of lack of absorption. These masses have continued in some cases for several months and on aspiration have been found to contain a high concentration of sulphetrone. Until, therefore, this problem, which is essentially a pharmaceutical one, is overcome, any sulphone in an oily medium which gives lack of absorption cannot be recommended. The parent substance, diamino-diphenyl-sulphone, in a suspension of arachis oil and of hydnocarpus oil has not generally shown these drawbacks.

Conclusion.—In conclusion, therefore, it is evident that all the sulphones have a definite action on the *M. lepræ* and the choice of the sulphone depends on three factors: (i) price, (ii) ease of administration, (iii) availability and absence of toxic effects or lack of absorption. Viewed in this light the preference at present must be given to a 50 per cent solution of sulphetrone in water. In view of the fact, however, that the oily medium may be more slowly absorbed, it would seem that work should be carried out on the production of an emulsion or a suspension which would be easily absorbed. Diamino-diphenyl-sulphone, in our opinion, is the most effective anti-leprosy remedy which we have used, but until the question of toxicity is settled it is not at present advisable to use it.

Thioarsenites in Amœbiasis: A Clinical Appraisal of New Amœbacides

(From the *Journal of Tropical Medicine and Hygiene*, Vol. 53, January 1950, p. 19)

At the beginning of World War II, a number of articles appeared on the therapy of amœbiasis, in anticipation of an increasing need for control. These were largely generalizations on the use of drugs introduced within the carbarsone, vioform and diodoquin (diiodohydroxyquinoline). Nelson stated, '...when a number of different agents are in use in the treatment of a particular pathologic state or infection, none of the agents is completely satisfactory. In no field is this more true than in the treatment of amœbiasis'.

Emetine, long held by the British to be effective, either as the hydrochloride for parenteral use or as the bismuth iodide for oral administration, should not be considered a curative agent. It will control symptoms of acute dysentery and hepatitis, because it accumulates in the liver. The encysted forms of *Entamoeba histolytica* are not killed by therapeutic levels of emetine in any form. Relapse is the rule rather than the exception after this drug is used alone, regardless of total amount given and duration of therapy. It is recognized that when emetine is employed patients should be hospitalized and care must be taken to avoid possible damage to cardiac muscle.

Amœbiasis, as it is known in the Western hemisphere, is essentially a chronic recurrent infection which may remain dormant for years. Some agent other than emetine is required for control and complete eradication of the cysts as well as the motile forms of *E. histolytica*. According to Adams, in his writing of British experience with the disease, this basic distinction has not been recognized generally. The common practice, in some areas, of giving periodic courses of emetine should be discouraged because of the possibility of development of drug-resistant strains.

Historically, the halogenated hydroxyquinolines, beginning with Mühlens' and Menk's introduction of chiniofon (as yatro) in 1921, vioform by Anderson and Koch, in 1931, and diodoquin by Tenney in 1936, have had considerable vogue as amœbacides. Despite recent reversals of early opinions of effectiveness they still are used extensively, almost always in high dosage and with other agents. The United States Navy's refusal to include diodoquin among essential medical supplies during World War II is a reflection of the criticism being levelled against this agent. David and his co-workers, in commenting on the toxic effect of diodoquin as described by Silverman and Leslie, described the uncontrolled oral use of amœbacides. Like other available agents, they are potentially toxic, and David, Phatak and Zener have shown iodine levels in the blood after oral use of diodoquin. These ranged from 45.6 to 437.25 micrograms per hundred millilitres. It is not known what proportion of this is free iodide and whether diodoquin exists as such in clinically effective amounts. Appreciable, but lower, iodine levels in the blood followed vioform medication over a ten-day period. It is possible that this compound does not break down as readily as diodoquin.

More recently, studies of the metabolism of chiniofon, utilizing radioactive iodine, have revealed that absorption of the halogenated hydroxyquinoline also occurs. The amount was small, however, and, according to Albright, Tabern and Gordon, averaged 12.9 per cent of the dose given. Absorption was prompt, the peak blood level appeared in two hours and the highest urinary level was found during the initial three hours after ingestion. The bulk of excretion occurred by the twelfth hour, and it was complete in forty-eight hours. However, free iodine was split off from the molecule and only 7.4 per cent of the total administered chiniofon was excreted as such. The belief was

expressed that blood levels of clinical importance could not be attained even with rapid absorption, because of the low percentage absorbed, the rapid urinary excretion and the body's ability to break down the drug into free iodide and organic rings.

The other chemical types most extensively used include the arsenicals, carbarsone and acetasone. Marchoux's early introduction of acetasone (as stovarsol) was responsible for its trial in this country. Bender and others have shown frequent cutaneous and other reactions to therapeutic doses which have led to its abandonment for general use as an amœbacide in the United States. Thus carbarsone among agents in this class has enjoyed most widespread use and is considered by most authorities as a safe agent in the absence of contra-indication to arsenical therapy. For the majority of patients, carbarsone, alone or in combination with agents of different chemical types, is satisfactory. Experience during the recent war revealed that doses larger than originally recommended can be used even under field conditions. Hakaussan anticipated this in 1935.

It has been observed that, in certain patients who have been treated for relief of symptoms alone and because of inadequate follow-up, chronic re-entrant relapsing amœbiasis has developed. In addition, there are patients who have had the disease for years, with varying degrees of invalidism, who have had no specific therapy and who present a therapeutic problem from the outset. Mackie and his co-workers, in a recent survey of selected war veterans in North California, has shown that among 363 persons adequately examined 40 per cent had amœbiasis. He stated, '...almost without exception these persons were having symptoms of sufficient significance to interfere with their activity'.

Palmer, in an excellent follow-up study of a group of 40 veterans, said that clinical observations on wartime military amœbiasis were hampered by the constant necessity for moving the patient from one area to another, with the result that final evaluation of the long-range results of therapy was not possible. His report of results on conventional treatment schedules, with an average of two and a half months' observation after 'cure', emphasized the tendency for remission or exacerbation to occur during observation. The persistence of colon tenderness and diarrhoea, without blood, in patients not passing amœbæ or showing evident pathologic changes on sigmoidoscopic examination was not uncommon. Only 2 of 40 patients had spontaneous remissions and could not be found to harbour *E. histolytica* during the period of observation. Blunderbuss therapy of the remainder, in which a total of sixty-two courses of treatment were required, brought about some semblance of control. It was concluded that there was no apparent relationship between size of drug dose and its effectiveness in amœbic colitis.

The experiences cited indicate dissatisfaction and lack of agreement regarding the therapy of amœbiasis. It was for this reason that the present study was started in 1944, with the hope of developing a more effective amœbacide than any now available. The results of the preliminary studies, leading to the current work with the thioarsenites have been reported elsewhere. In excess of 250 agents have been examined, representing a variety of chemical types, with *in vitro* and *in vivo* techniques developed at the University of California in 1931.

One hundred patients harbouring *Entamoeba histolytica* and other parasites in Memphis, Tenn., and San José, Costa Rica, were treated with either p-carbamidophenyl-bis (carboxy-methyl-mercapto) arsine or p-carbamidophenyl-bis (2-carboxyphenylmercapto) arsine. These agents, in previous laboratory studies, proved approximately ten times more effective than carbarsone U.S.P., in both *in vitro* and *in-vivo* tests (in naturally infected macaques).

Of 82 patients, 77 with *E. histolytica*, 3 with *Disentamoeba fragilis* and 2 with *Balantidium coli*, 74 were

cleared of their parasites over a four-month follow-up period. Eighteen others, infected with *Dientamoeba fragilis* (2), *Strongyloides stercoralis* (12), *Fasciola hepatica* (1), *Leishmania tropica* (2) and *Treponema pertenue* (3) had no significant benefit following thioarsenite therapy.

Complete clinical appraisal before, during and after therapy, including tests of urine, blood and hepatic, renal and heart functions, revealed no drug toxicity due to the dose levels employed (3.0 grammes orally in ten days to 7.2 grammes in twenty-four days). In addition, 13 of these patients with acute dysentery also received C.C. 1037 in retention enemas (3.0 to 6.0 grammes in six days) with benefit and without evidence of drug toxicity to mucous membranes of the lower bowel as revealed by protoscopic examination. No cutaneous reaction or damage to other tissues was observed. Twelve patients exhibited nausea or vomiting after 200 mg. doses of either thioarsenite. Coating of the tablets with phenyl salicylate permitted completion of therapy in all but 1 of these patients.

Three Costa Rican patients with hepatitis, who had evidence of sulphobromophthalein sodium retention (5 to 20 per cent) at 45 minutes (before therapy) were cleared of amœbæ, and their hepatic function returned to normal. One of these also required emetine hydrochloride, 0.5 gramme given parenterally over five days. Bismuth subcarbonate was also given to 2 other patients with long-standing dysentery.

Since earlier laboratory experience was confirmed, i.e. the thioarsenites are tolerated and effective in dose levels from one-tenth to one-fifth those of carbarsone, it is suggested that enteric-coated tablets of 25 to 50 mg. be employed orally, on a three times daily dose schedule over ten days. The thioarsenites in retention enemas may also be required in patients with severe dysentery.

It would appear, on the basis of laboratory and clinical trials, that the detoxication of carbarsone oxide (p-carbamidophenylarsenous oxide) by substituted sulphhydryl groups has permitted the use of active trivalent analogues of carbarsone U.S.P. with greater distribution of an active agent to tissues, such as the liver and intestinal tract where amœbic invasion occurs.

A Simplified Procedure for Blood Cell Counts and Hæmoglobin Determination

(From the *Physician's Bulletin*, Vol. 14, November-December 1949, p. 179)

A VERY ingenious method for diluting blood for blood counts is described by Wroblewski, Weiner, and Shapiro, of the New York College of Medicine and Goldwater Memorial Hospital. In the method described, the numerous pipettes required for repeated blood determinations are replaced by capillary tubes that can be quite easily prepared. The principle of the method was originally described by Goldfeder *et al.* (*Proc. Soc. Exper. Biol. and Med.*, 67, 272, 1948).

Capillary tubes are prepared and calibrated to contain the amount of blood equal to the 0.5 mark of the Thoma blood-cell pipette. A capillary tube is filled with blood which has been obtained by finger puncture and then diluted with a volume of diluting fluid (Hayem's solution for red cells, 2 per cent acetic acid for white, 0.1 N hydrochloric acid for acid hæmatin formation). The blood count or hæmoglobin determination is made in the usual fashion by using a Neubauer Briteline counting chamber and Sahli hæmometer.

Mercury is drawn into a standard Thoma white-cell pipette up to the 0.5 mark, and the measured volume of mercury is transferred into a length of capillary

tubing through a wide end. The lengths of capillary tubing containing the measured amount of mercury are marked off with a diamond-point pencil, and these calibrated lengths are then separated into individual tubes. Thus, each capillary tube contains exactly the same volume of blood ordinarily drawn into the white cell pipette up to the 0.5 mark. Capillary tubes for the red cell and hæmoglobin determinations are prepared by the same technique with the corresponding pipettes. By this technique, a large supply of calibrated capillary tubes can be prepared at one time.

Diluting fluid (Hayem's solution) is drawn into a standard red-cell pipette up to the 101 mark and then transferred to a small test-tube (75 × 10 mm.). The finger tip is punctured. A calibrated red-cell capillary tube, held in a pair of forceps, is touched to the blood obtained from the finger tip; this results in immediate filling of the tube by capillary action. The blood-filled capillary is then dropped into the test-tube containing the diluting fluid, and mixing is readily accomplished by shaking. A drop of red cell suspension is then transferred to a counting chamber by means of a glass rod or applicator stick, and the cells are counted by the usual method.

The method is in every way identical with that described for the red cells, except that the corresponding diluting fluid (2 per cent acetic acid), diluting volume, and calibrated white-cell capillary tube are used.

For hæmoglobin determinations, dilute (0.1 N) hydrochloric acid is added to the comparison tube of the Sahli hæmometer in the usual manner. Blood is obtained from the finger tip with a calibrated hæmoglobin capillary tube, and the blood-filled capillary is dropped into the comparison tube, which is then shaken to accomplish mixing. Distilled water is added until the colour matches the standard.

The advantages of the capillary-tube method described are especially apparent in hospitals and clinics, where many blood counts are done daily. Only one set of pipettes is required for any number of complete blood counts.

The tubes may be re-used indefinitely after they have been placed in a detergent or in a cleaning solution, rinsed and dried. The capillary-tube method permits all the measuring of diluting fluid to be done in the laboratory at one time, away from the patient and the bedside, and simplifies the blood sampling.

There is no problem of obtaining too large or too small a quantity of blood by missing the mark. The technique of capillary filling works as well on oxalated blood as it does on finger-tip blood. The procedure is highly economical because it eliminates the need for large numbers of blood-cell-counting pipettes. The cost of capillary tubes is negligible.

The Action of Mercurial Diuretics in Congestive Cardiac Heart Failure

(From the *Medical Journal of Australia*, Vol. II, 17th December, 1949, p. 888)

THE use of mercurial diuretics in congestive cardiac failure is now standard practice, and provided the renal function is satisfactory, other forms of œdema are now safely treated by these drugs without any of the fears once entertained by unadventurous therapists. The inclusion for injection in the British Pharmacopœia of mercurial preparations now emphasizes their everyday usage, and perhaps curiosity as to their action is somewhat languid. The official preparation contains sodium mersalylate in 10 per cent aqueous solution with the addition of 5 per cent theophylline. L. G. C. Pugh and V. L. Wyndham have set out to determine what are the circulatory effects of this combination, and have contrasted its action with that of the mercury salt:

alone. It is generally agreed that the diuretic effect is due to a direct action of the mercurial salt on the kidney, by which the reabsorption of water and salt from the distal convoluted tubules is lessened, but the circulatory effects are less understood, especially as the position is complicated by the adjuvant action of another drug. Pugh and Wyndham carried out studies on eleven patients under treatment for various types of congestive heart failure. Most of them were seriously distressed by dyspnoea and oedema, and the venous pressure was greatly raised. It follows that extensive investigations were not always possible, but in every instance cardiac catheterization was performed, the pressure in the right auricle was estimated, and gas analyses of its contained blood were made. Oxygen consumption was measured directly or by spirometry, and the cardiac output estimated. A dye method for determining the blood volume was not found very satisfactory, and in some cases an attempt was made to estimate it during the experiment by observing the hæmoglobin content of the blood. Hourly measurement of the heart rate, blood pressure and urinary volume was made. In order to control the effect of the theophylline in the preparation, a special mercurial injection was prepared by the makers of the standard injection, and this was used without any addition of theophylline. The authors compared the findings with the results of venesection and found that the circulatory effects were similar, but of course there was a distinct difference in time, as venesection, or such a procedure as constricting the thighs by cuffs, acted much more quickly. In general it was found that the cardiac output rose, and the pressure in the right auricle fell. These effects began to be evident after two hours, and reached their peak in five to seven hours declining and disappearing as the urinary output diminished once more. These findings applied to the use of mercurial diuretics with the addition of theophylline. When the pure mercurial alone was employed the rapid fall in intra-auricular pressure was not seen, nor was the transient increase in the cardiac output, though a slow rise in output of the heart, accompanied by a fall in pressure in the right auricle, occurred later as diuresis was established. The quick response was apparently due to the theophylline. All details of the changes which occur after this form of treatment have not yet been worked out and the authors think that more work is needed before the mechanisms are clearly revealed. It would appear, however, that the immediate effect of mercurial diuretics on the circulation *per se* are slight, and those which can be detected later are due to the relief given by diuresis. The retention of the theophylline in the official preparation would seem to be justified, even if the effect is transient. One point mentioned by the authors is that they thought it advisable to reduce the dose of the mercurial when given alone, recognizing the toxic nature of the drug, for they point out that sudden death has occurred after the injection of a mercurial preparation, and it is possible that a sudden lowering of venous pressure may be an occasional vagary in its action on the circulatory system.

The following 3 items are reproduced from Medical Newsletter No. Wa 260, May 1950, prepared by the American Medical Association :

(1) Management of the Symptom Complex in Acute Poliomyelitis

SMITH and his associates in analysing poliomyelitis from the point of view of pathologic physiology, emphasize the rôle of the sympathetic nervous system.

Because of the feeling that much of the pain and spasm in acute poliomyelitis was due to the spread of waves of nervous excitation along the sympathetic

nerves with resultant vasoconstriction and ischemic changes, it was decided to direct therapeutic attempts at blocking or interrupting these pathways. The drugs used were procaine hydrochloride, diethylaminoethanol hydrochloride, and priscoline.

The authors employed priscoline in 120 patients. It produced the best results when the patient experienced a sensation of warmth or when the skin flushed. Priscoline was given intramuscularly in case of acute pain, hyperæsthesia or muscle spasm.

In those over 16 years of age the initial dose was 50 mg. If the patient flushed, he was given 50 mg. every three or four hours. However, if he did not flush, the dose was increased 12.5 mg. every three or four hours until the amount necessary to produce the flush was found. This amount or the next smaller dose was then used as a maintenance dose. As soon as the pain and muscle spasm subsided, oral priscoline was substituted. The oral dose was usually higher than the intramuscular. For children between 5 and 16, the initial dose was 25 mg. and to children below five years of age elixir of priscoline was given, the initial dose being 10 mg.

Priscoline caused no serious secondary effects, except that 5 per cent of the patients had nausea and vomiting. Repeated examinations of blood and urine revealed no changes. The longest period of administration of priscoline was seven and one-half months.

The drug produced a sense of well-being. The patients rested more comfortably during the day and slept quietly at night. The appetite improved. The acute pain subsided quickly, and extremities, flexed because of pain or spasm, were easily straightened. Muscle twitchings quickly disappeared. The cold and clammy skin became warm. Nearly all the patients improved so rapidly that it was possible to transfer the majority, relaxed and free of pain to their homes or orthopaedic hospitals in from 7 to 14 days.

(Smith, E., Brooklyn, N. Y., Graubard, D. J., and Rosenblatt, P.: *New York State Journal of Medicine*, 49, 2655-2660, November 1949. The authors are connected with the Communicable Disease Service and Department of Laboratories, Kingston Avenue Hospital.)

(2) Measles Encephalitis : Study of 50 Cases

SAWCHUK and his associates say that during winter and spring of 1946 a severe epidemic of measles took place in Philadelphia, during which 13,037 cases were reported to the Health Department. There were 14 cases of measles encephalitis, a ratio of 1 to 1,000. The cases of the last 50 patients with measles encephalitis, including the 14 of 1946, treated at the Philadelphia Hospital for Contagious Diseases, were reviewed and analysed. Sixteen of the 50 patients died, a mortality rate of 32 per cent. Many of the patients had complications in addition to the measles encephalitis; 18 also had pneumonia.

Studies on the spinal fluids indicated that a low spinal fluid cell count (less than 50 cells) in measles encephalitis indicates a grave prognosis.

The authors present their experiences with dehydration therapy, which consists of the limitation of fluids given by mouth and the administration of hypertonic glucose solution intravenously, hypertonic magnesium sulphate enemas and concentrated human plasma intravenously. Because of the danger of complicating bacterial infection, prophylactic chemotherapy was instituted early in the disease. Except for sulphonamide drugs, used in a few of the early cases, penicillin was the drug of choice. When the results of dehydration therapy are compared with those of non-dehydrating therapy, it is evident that the small difference in the percentage of mortality is not statistically significant. In certain instances, dehydration therapy seemed to prevent further involvement of the brain, but this was not so in every case.

Neurologic and psychologic examinations were made on 19 of the 34 surviving patients. Of the 19 patients examined, only two were normal, psychologically and neurologically. The greatest number of neuromuscular disorders involved the extremities; most of the others involved the cranial nerves. Each child with mental deficiency had also one or more neurologic abnormalities. Four of the mentally defective patients had electroencephalograms made, three of which were abnormal.

The authors present the pathologic changes observed in nine patients with central nervous system disease complicating measles who came to autopsy. The gross picture of encephalitis complicating measles is suggested by oedema, engorgement of the superficial meningeal vessels and prominence of the smaller vessels in the white matter. An occasional case may show perivascular staining indicating focal hæmorrhages. The brain is heavier than normal, and the convolutions are flattened as a result of the oedema. In some cases a cerebellar herniation cone may be present and may account for central cardiorespiratory failure. Again, these gross changes are not specific, as they may be seen in any of the encephalitides and may be present in circulatory insufficiency or failure.

The authors stress the non-specificity of the gross and histopathologic features in order to emphasize the importance of the clinical evaluation.

Only 2 of 19 patients given follow-up study were perfectly normal by electro-encephalogram and neurologic and psychologic examination.

Fourteen of the 19 patients given follow-up study have minor sequelæ involving the extremities.

(Sawchuk, S., Philadelphia, Pa., LaBocchetta, A. C., Tornay, A., Silverstein, A., and Peale, A. R.: *American Journal of Diseases of Children*, 78, 844-867, December 1949. The authors are connected with the Philadelphia Hospital for Contagious Diseases.)

(3) Erythroblastosis Foetalis. V. The Value of Blood from Female Donors for Exchange Transfusion

IN reviewing the data from 208 cases of erythroblastosis foetalis treated by exchange transfusion, Allen and associates were surprised to note that although the mortality was over 15 per cent in the whole group, there were no deaths in a group of 42 babies who happened to receive blood from female donors exclusively. This prompted the examination of available data in this large series.

The sex of the blood donor was included in the records only as an after-thought, the interest of the authors being turned in this direction by their recent observation that female babies with erythroblastosis foetalis do significantly better than male babies, especially with regard to the incidence of kernicterus. Since the discovery that blood from female donors seemed to be superior for exchange transfusion in infants with erythroblastosis foetalis, the authors have chosen women as donors deliberately for 13 babies with this disorder and none of these 13 died. The beneficial effect of blood from female donors has been shown to result only from the use of relatively large quantities (150 cc. or more).

The beneficial component of the blood from females is not known, but isolated plasma fractions are being investigated. It appears that, for the present, exchange transfusion, using blood from a female donor, is the treatment of choice in babies with erythroblastosis foetalis.

It is possible that further statistical data will not substantiate the analysis here presented. At any rate, the beneficial effect of exchange transfusions using blood from female donors can be quickly ascertained from a brief study of current and past records in a number of clinics. It is hoped that such studies will

be done. The potential value of a beneficial component of blood from female donors may not be limited to babies with erythroblastosis foetalis, and a preliminary study of other groups of babies requiring and receiving transfusion is promising.

(Allen, Jr., F. H., Diamond, L. K., and Watrous, Jr. J. B.: *The New England Journal of Medicine*, 241, 799-806, November 1949. The authors are connected with the Blood Grouping Laboratory of Boston, Children's Medical Centre, Boston, the Boston Lying-in Hospital, and the Departments of Pædiatrics and Obstetrics, Harvard Medical School.)

A Study of the Effects of Malaria and of Malaria Control Measures on Population and Vital Statistics in Kanara and Dharwar Districts as compared with the Rest of the Province of Bombay

By D. K. VISWANATHAN

(Abstracted from the *Indian Journal of Malariology*, Vol. 3, March 1949, p. 69)

THE effects of malaria on growth of population are discussed. In the hyperendemic portion of Kanara, there is a progressive decline from 1881 to 1941. In the coastal portion of this district and in Dharwar district, there is a progressive increase than in the rest of the province but the difference is not significant.

Hyperendemic malaria reduces birth rate by about 5 per mille, increases malaria death rate by about 0.75 to 1 per mille. Total death rates are only slightly raised presumably due to better economic conditions.

Rural malaria control on an extensive basis has helped to reduce morbidity greatly, increase birth rates by about 5 per mille and only slightly, if at all, decrease total death rates.

Malaria death rates are greatly reduced.

In areas where cattlesheds are sprayed, deaths due to diarrhoea and dysentery are also reduced and in the entire area plague has been absent.

It is estimated that in 30 years there will be 10 per cent more of adult population available for land development and every year at least 250,000 labour days saved from sickness.

These changes make it desirable to consolidate still further by extending the benefits to smaller villages at additional expenditure which will however be more than repaid in increased food production to a far greater extent than in many similar areas but peopled with more backward classes.

A plea is made for an economic survey of the villages under malaria control and without, respectively, so that further useful data may be made available on the economic advantages of malaria control.

Indian Curds or 'Dahi' as a Source of Vitamin B Complex and Growth Factors

By N. V. JOSHI

(From the *Indian Journal of Medical Sciences*, Vol. 4, February 1950, p. 81)

IN the course of our investigations on the organisms in Indian curds or 'dahi', we found a species of yeast of the genus *Torula* which we consider to be an

entirely new one because of the biochemical reactions and physiological activities displayed by it and hence the new *Torula* is named by us as '*Torula dahi*' (nov. sp.).

'*Torula dahi*' was found in all the samples of '*dahi*' examined at a number of places all over India. In fact, Indian curd may be considered to be its natural habitat. Its function in our curds is rather interesting. It supplies vitamin B complex for the proper growth of the lactic acid bacteria, which turn our milk sour. By the method of microbiological assay we were able to show that this yeast produces riboflavin, nicotinic acid, biotin, thiamin, pyridoxin, p-amino-benzoic acid and folic acid. In the several extracts of the cultures of this *torula*, each of the above constituents of vitamin B complex and growth factors, was found in sufficient quantity to meet the full requirements of lactic acid bacteria. Only pantothenic acid was slightly less than the usual quantity required for the growth of the lactic acid bacteria.

It is generally recognized that the bacteriostatic effect of some of the sulpha drugs like 'sulphanilamide' are counteracted by even a small dose of p-amino-benzoic acid. In view of the fact that when we take curds with our rice or in a diluted form as 'maththa', 'lassi' or 'chaas' as a drink or during our meals, we consume not only lactic acid organisms but also '*Torula dahi*', which produces vitamin B complex and p-amino-benzoic acid, etc.

In view of the above information the possibility suggests itself that sulpha drugs might prove ineffective in the case of patients, to whom these drugs are administered, if they happen to take a diet in which curds or other preparations of curds are included.

We wonder if any such effect has been observed in making the action of sulpha drugs, sulphanilamide, for instance, ineffective because of the patients consuming curds or '*dahi*' and if so whether the physicians would consider the desirability of stopping curds in any form to the patients who are under treatment with sulpha drugs.

Plasma Protein Levels of Healthy Indian Subjects

By G. N. GOKHALE

and

R. G. CHITRE

(Abstracted from the *Indian Journal of Medical Sciences*, Vol. 4, February 1950, p. 48)

PLASMA protein levels of 40 healthy adult male Indian subjects were estimated by Howe's method.

Plasma protein values with standard deviations are given below in g. per cent plasma:—

Total protein	6.93 ± 0.47
Albumin	4.70 ± 0.35
Globulin	2.26 ± 0.38

Erythrocyte sedimentation rate, hæmoglobin, packed cell volume and red blood corpuscle counts were investigated in detail in six subjects. The plasma protein levels of these six healthy adult male Indian subjects compares well with the 40 cases studied in the present series.

Hæmoglobin, packed cell volume, and red blood corpuscle counts made by the standard methods and these obtained by calculations from the specific gravities of blood and plasma show close relation but not concurrence.

A Case of Severe Generalized Reaction to Mosquito Bites

By W. CREWE

and

B. G. MAEGRAITH

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 42, January 1949, p. 317)

It is well known that in certain instances severe generalized manifestations may occur in sensitized subjects as the result of bee and wasp stings, but such general reactions are seldom reported following the bites of blood-sucking insects. A reaction of this type was exhibited by a patient suffering from falciparum malaria who, in an attempt to infect mosquitoes, was exposed to the bites of 380 *Anopheles maculipennis* and 20 *A. stephensi*.

The clinical report on this patient was as follows:—

History of several previous attacks of malaria. Admitted 5th August, 1948, suffering from falciparum malaria acquired in West Africa. Treated with paludrine 300 mg. b.i.d. for 10 days. Asexual parasites absent from blood by third day of treatment. Gametocytes persisted. *Entamoeba histolytica* cysts present in stool. Treated with standard 3 weeks' course. After treatment for amœbiasis, falciparum gametocytes were still present and it was decided to attempt to infect *A. maculipennis* and *A. stephensi*.

7th September, 1948.—Four hundred mosquitoes (*A. maculipennis* except for 20 *A. stephensi*) were fed on patient's thighs in 28 minutes. Most mosquitoes fed. (No mosquitoes became infected.)

Ten minutes after feeding began, patient noticed epigastric pain followed by 'flushing' radiating upwards to back of neck and down arms and later legs. He felt his heart pounding and noticed his vision was blurred. Large itching wheals developed on both thighs where feeding had taken place—more pronounced on left, where *A. stephensi* had fed. Wheals also appeared on neck and arms, particularly at the wrist and flexure of the elbow joints. The skin of the face, including the conjunctival vessels, the trunk, arms and legs became deeply flushed.

At this stage the pulse rate was 150 per minute, the pulse full and bounding, and the blood pressure 80/40. There was no appreciable rise of temperature. Stroking of the skin failed to elicit a white line response.

The administration of anthisan 0.1 gramme orally was followed by marked improvement associated with a slowing of the pulse rate to 90 per minute and a rise in blood pressure to 120/70. Flushing of the skin faded in 3 hours except over the region of feeding. A further dose of anthisan 0.1 gramme was given 5 hours later. The wheals in the feeding area persisted for 24 hours. Two days later there were numerous small red papules scattered over the site of the mosquito bites. The patient was well except for occasional headaches.

Management of Anuria

By A. MILLER

(Abstracted from the *British Journal of Urology*, Vol. 21, September 1949, p. 243)

Causes of anuria.—The most suitable classification is that of Swift Joly, which divides causes into pre-renal, renal, and post-renal.

Pre-renal implies cessation of urinary secretion due to a fall in blood-pressure below the level which will maintain an adequate filtration pressure in the glomeruli, which may be due to a diminution of the circulatory blood volume (e.g. hæmorrhage, dehydration) or to a slowing of the circulation rate (e.g. cardiac failure).

By *renal* causes he meant stoppage of secretion in the presence of adequate filtration pressure and with unobstructed ureters. In these cases tubular damage or blockage occurs (e.g. crush syndrome, incompatible blood transfusion, sulphonamide intoxication); it is probable that the glomerular filtrate is almost all reabsorbed direct into the blood stream owing to the destruction of the cell lining the tubules.

Post-renal means ureteric obstruction (e.g. calculous anuria, or sulphonamide crystal blockage). This can be differentiated from the other two varieties by ureteric catheterization.

The functions of the kidney which are lost are:—

1. *The power of secreting water*; this means that the skin, lungs, and bowel remain as the only means by which the body can get rid of excess water, and the total amount excreted by these channels does not normally exceed 1,000 ml. a day.
2. *The excretion of the products of protein breakdown*, of which urea forms the bulk and is the most easily measured indicator.
3. *The maintenance of the normal electrolyte balance and osmotic pressure of the blood*, by excretion of excess acid or base as required, and variation of amounts of fluid reabsorbed.

Three phases.—It is possible to regard the natural course of these unobstructed cases of lower nephron damage as falling into three phases: The *first*, in which renal failure is determined and which lasts a few hours or less, followed by the *second* phase in which life continues in the absence of renal function, the blood urea mounts by 20 to 30 mg. per cent daily and electrolyte disturbances gradually increase and produce a tendency to acidosis. During this phase epithelial regeneration is occurring in the tubules, and when this reaches amounts adequate to prevent reabsorption of the filtrate (usually about the eighth day) the *third* phase or period of recovery starts with the production of urine. In other words, the kidneys recover spontaneously or not at all by a normal process of regeneration of damaged epithelium; therefore, when the kidneys are not working, fluids must not be given in amounts which exceed the insensible loss, and no attempt should be made to force the kidneys to secrete which interferes with the water and salt balance or which prevents regeneration of tubular epithelium. These two principles present the basis of successful management of temporary renal failure.

The results obtained by employment of established methods of treatments were discussed, including intravenous sodium sulphate in 4.285 per cent solution. It was found that this merely increases the level of sodium and sulphate in the blood and cannot have any effect unless urine production is proceeding normally. Other diuretics were also abandoned for this reason.

SCHEME OF MANAGEMENT

First phase.—1. Restoration of blood volume, blood-pressure, and hæmoglobin level to as near normal condition as possible by transfusion.

2. Cystoscopy and catheterization of both ureters; if obstruction is found and cannot be relieved by simple measures (as in blockage by sulphonamide crystals), it is better to perform nephrostomy than to attempt a definitive operation such as uretero-lithotomy.

3. Estimation of blood sodium, chloride, bicarbonate, and urea.

Second phase.—1. Limitation of fluid intake to approximate to insensible loss, about 1 litre daily.

2. Low protein, high carbohydrate diet.

3. Maintenance of adequate hæmoglobin level by transfusion.

4. Checking of progress by estimating blood urea and blood bicarbonate levels on alternate days.

5. Employment of dialysis if generalized œdema is present, or blood urea has risen to 200 mg. per cent.

Third phase.—1. Fluid intake made to balance fluid loss in urine added to insensible loss.

2. Salt intake made to balance salt excreted in urine. Half daily volume of urine excreted indicates approximate amount of normal saline required by mouth.

3. Checking of progress by estimating blood sodium, chloride, bicarbonate, and urea every two to three days until diuresis subsides.

Histoplasmosis and Tuberculosis

(From the *Medical Officer*, Vol. 83, 21st January, 1950, p. 25)

THERE was a time not so long ago, when many, perhaps most, radiologists or tuberculosis physicians labelled with confidence as tubercular a great many abnormal or obscure shadows present in x-ray films of the lungs. The 'enlarged hilar gland' ramp is not yet forgotten.

In parts of the United States of America pulmonary calcifications occur in many persons who are not hypersensitive to tuberculin, but are hypersensitive to histoplasmin. From some of these the fungus *Histoplasma capsulatum* has been recovered. The latest study of this interesting subject is by Michael L. Furcolow, M.D., published in No. 44 Public Health Report of the United States Federal Security Agency, and entitled Development of Calcification in Pulmonary lesions associated with sensitivity to Histoplasmin.

The pulmonary calcifications in the two diseases are indistinguishable in appearance but some occur in tuberculin sensitive and others in histoplasmin sensitive persons. It is known as regards tuberculosis that the antecedent lesion is a pulmonary infiltration in a tuberculin positive individual from whom it is possible sometimes to recover the mycobacterium tuberculosis.

Similar infiltrations have been found in histoplasmin positive, tuberculin negative persons, and the way calcification develops in such lesions has now been shown and shown convincingly by Dr. Furcolow. Periodic routine school x-ray and skin testing surveys in Kansas City disclosed several hundred histoplasmin positive, and tuberculin negative children with pulmonary infiltrations. These lesions (described in 1947 by Furcolow, Mantz, and Lewis, Public Health Report No. 62) were followed up for varying periods up to four years, during which time some of the infiltrates disappeared completely, some apparently became fibrotic, but the majority gradually developed calcification. These changes are recorded in good reproductions of some fifty-six skiagrams. Infection with the fungus *Histoplasma capsulatum* may therefore give rise to changes in the lungs which by radiography resemble tubercular pulmonary infiltrations. Histoplasmosis was at first held to be a rare and usually fatal disease, but is now known to be common in certain parts of the world, and to exist in a mild form apparently without symptoms. The moral is at least clear. No diagnosis of tuberculosis must ever be made on x-ray evidence alone.

Reviews

SYPHILIS: ITS COURSE AND MANAGEMENT.—By E. W. Thomas, M.D. 1949. The Macmillan Company, New York. Pp. 317 with 67 Illustrations. Price, 42s. net

This book is revolutionary in its outlook on the treatment of syphilis. So appears to regard it the writer of the foreword, who hopes that the author in a series of revisions will attempt a final evaluation of the events now taking place.

The book is based on results of ten years of intensive therapy and five years of antibiotic therapy. The observations have been made at Bellevue Hospital, New York, and in the New York State prisons.

Typical opinions are: (1) Spontaneous cure may occur in 28 per cent of untreated cases. (2) Without treatment infectious relapses of early syphilis will not occur after two years; with inadequate treatment they may occur for five years at least. (3) Latent syphilis is not an emergency. The diagnosis should not be made in haste. (4) There is no reason to believe that latent syphilis requires the amount and duration of treatment formerly advised. Observations on more than 3,000 prisoners for more than 10 years have shown that no patient who had 20 arsenical and 20 bismuth injections for latent syphilis developed demonstrable late symptomatic syphilis. (5) The majority of patients with untreated latent syphilis shows no signs of the progress of the infection. The purpose of treating latent syphilis is to prevent progression in the 25 per cent who, without treatment, might develop manifestations. (6) There is no reason to use arsenic at all except in cases where the disease fails to respond to penicillin. (7) Penicillin is the drug of choice for all stages of syphilis. Bismuth, in advance, is useful when therapeutic paradox is feared. These are some of the pronouncements.

In spite of the optimistic outlook the seriousness of neurosyphilis, cardiovascular syphilis, complications of pregnancy and congenital syphilis is brought out in detail and effective treatment prescribed. Public health aspects are included.

The usual information on aetiology, general description of the course, immunology, STS (with emphasis on Kahn test), obtaining of cerebrospinal fluid, composition and mode of action of the therapeutic agents is given concisely.

The book should be of special interest in India, in view of the various drives against V.D., the pessimism associated with the drives, overtreatment of the patients and the cost of some of the drives not needed particularly.

The get-up is very good. The price could perhaps be lower.

An excellent publication.

S. D. S. G.

FUNDAMENTALS OF INORGANIC, ORGANIC AND BIOLOGICAL CHEMISTRY.—By Joseph I. Routh, Ph.D. Second Edition. 1949. W. B. Saunders Company, Philadelphia and London. Pp. x plus 346. Illustrated. Price, 16s. 6d.

This medium sized book gives more information on the subjects than many much bigger books. Though written specially for nurses it will be equally useful in other courses in which the fundamentals of inorganic chemistry, organic chemistry and biochemistry are taught.

Even medical men desiring to renew their acquaintance with their earlier studies could not make a better choice. In it they will find the latest information on Solutions, Electrolytes and Ionization, Hydrocarbons, Carbohydrates, Lipids, Enzymes, Nutrition, Vitamins and Hormones. Even the atom bomb and its useful by-products have been explained.

The book can also be recommended with confidence to the authorities who may be contemplating translation of scientific books from abroad.

The get-up is very good and price reasonable.

An excellent publication.

S. D. S. G.

LECTURES ON MEDICINE TO NURSES.—By A. E. Clark-Kennedy, M.D., F.R.C.P. With a Foreword by Miss Clara Alexander. 1950. E. and S. Livingstone Ltd., 16 and 17, Teviot Place, Edinburgh. Pp. viii plus 288 with 28 Illustrations. Price, 15s. 6d. net

In these lectures Dr. Clark-Kennedy aims at giving nurses an outlook on medicine which will be of help to them when attending sick patients. This plan is to describe certain common symptoms, interpret them in terms of disorder of function and explain the nature of the pathological process. Enough of anatomy and physiology has been included in order to make the nature of disease intelligible to his audience. The indications of treatment are given wherever necessary, but last few chapters are mainly directed to therapeutics. In this way he has given a vivid picture of medicine in a language which nurses can understand and remember, and in a manner which is likely to stimulate their further interest. We can thoroughly recommend this book.

R. N. C.

TUBERCULOSIS: A DISCUSSION OF PHTHISIOGENESIS, IMMUNOLOGY, PATHOLOGIC PHYSIOLOGY, DIAGNOSIS AND TREATMENT.—By Francis M. Pottenger, A.M., M.D., LL.D., F.A.C.P. 1948. The C. V. Mosby Company, St. Louis. Pp. 597. Illustrated. Price, \$12.00

The author looks upon tuberculosis as mildly infectious, primary infection as a vaccination, and the disease curable. Fifty years ago every phase of the disease was surrounded by ignorance and pessimism; to-day every phase is approached with greater knowledge, less uncertainty, and increased optimism. The early chapters of this book deal with phthisiogenesis and pathology, incorporating author's personal views. This is followed by an account of clinical tuberculosis in childhood with particular reference to epituberculosis. There is a discussion on the visceral neurology of pulmonary tuberculosis followed by chapters on diagnosis, complications, classifications, spontaneous healing and treatment. The author states that he has used tuberculin for the treatment of tuberculosis for fifty years with good results. This view may not be shared by all workers. The last two chapters deal with the application of diagnostic and therapeutic principles in clinical practice and 'Future Program' including vaccination against tuberculosis. The get-up, paper, printing and illustrations are good.

R. N. C.

ARTIFICIAL PNEUMOTHORAX IN PULMONARY TUBERCULOSIS.—By T. G. Heaton, M.B. (Tor.). Second Edition. 1947. The Macmillan Company of Canada Limited, St. Martin's Street, London, W.C.2. Pp. xvi plus 292. Price, 20s.

Physicians interested in the subject will be grateful to Mr. Heaton for this compilation and classification

of abstracts of over three hundred articles on artificial pneumothorax. They will understand thoroughly the mechanics of this potentially lethal treatment, and this book can therefore be recommended as a valuable guide. The best of modern thought on A.P. has been summarized, arranged in logical sequence and commented upon by the author. There are numerous references to the literature on all aspects of the practical procedure. Consideration of complications and their treatment is also exhaustive. A new chapter on pneumoperitoneum has been added in this edition besides revision of all sections.

R. N. C.

MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS. PARTS I AND II. WRITTEN IN BENGALI.—By Dr. Jotindra Nath Ghosal, L.M.S. 1956 B.S. (1949). Published by Mr. B. Ghosal, 83, Karbala Tank Lane, Calcutta 6. Pp. 742. Price, Rs. 12 only

THIS book, written in Bengali, consists of two parts, the first part deals with various drugs and the second includes diet, nutrition, vitamin hormones, sera and vaccines, antibiotics, radium, electrotherapy, etc. The author has incorporated his own experiences in practice of medicine wherever possible. For instance in treatment of malaria he never had to give more than 5 grains or quinine in one dose or more than 15 grains in one day throughout his private practice. The reviewer agrees with the dosage especially in endemic areas of this country. But the administrations of a tonic pill containing quinine and plasmoquine two or three times a day may not be safe. Many terms have been written in English and an English index has also been included for easy grasp and reference.

R. N. C.

ERRATA

In the *Indian Medical Gazette*, 84, August 1949, p. 373, column 2

- (1) under PRACTICE OF MEDICINE, line 5—
for Pp. 354 read Pp. 738.
- (2) under SHISHU-O-STREE CHIKITSA, line 6—
for Pp. 171 read Pp. 460.

BOOKS RECEIVED

1. Immunity Bulletin. Commemorative Volume, April 1950. Founder: (Late, C. N. Dutta, M.B. Published by Dr. T. N. Ghosh, D.Sc., A.L.Sc., and Dr. A. N. Bose, M.B., Joint Secretaries, Immunity Scientific Association, Bengal Immunity Research Institute, 39, Lower Circular Road, Calcutta 16.

2. A Summary: Topographical Account of Scrub Typhus, 1908-1946. By J. R. Audy. Bulletins from the Institute for Medical Research Federation of Malaya. No. 1 of 1949. Kuala Lumpur: Printed at the Government Press.

3. A Malaria Parasite of the Malayan Squirrel. By John W. Field and J. F. B. Edeson. Bulletins from the Institute for Medical Research Federation of Malaya. No. 2 of 1949. Kuala Lumpur: Printed at the Government Press.

4. An Epidemic of Typhoid Fever due to Ice-Cream. By R. Green and D. S. Mankikar. Bulletins from the Institute for Medical Research Federation of Malaya. No. 3 of 1949. Kuala Lumpur: Printed at the Government Press.

Correspondence

KALA-AZAR IN INDIA AND THE SANDFLY

To the Editor, 'Indian Medical Gazette'

SIR,—I write to draw attention to three articles on the transmission problem of kala-azar which have appeared in your journal in recent years, namely:—'The Case Against the Sandfly' by Malone and Brooks (1944), a 'Reply' to that paper by Shortt (1946) and a 'Rejoinder' by Malone (1947). There were long intervals between the publication of the papers and their disjointed appearance detracts from their interest. To appreciate the full implications of the arguments, for and against the sandfly theory of transmission, the three papers should be studied side by side. Lack of space forbids a detailed consideration of all the points discussed in them, but I give here the gist of the main arguments in a much-abridged form. At the same time the reader is earnestly requested to refer to the original articles to ensure that I have 'played fair' in presenting the arguments of the eminent research worker who champions the sandfly theory of transmission.

I. After stating the admitted fact that *P. argentipes* must live 10 days or longer to transmit kala-azar in experimental (and presumably natural) conditions, we (Malone and Brooks) quoted the experiments of Smith *et al.* (1936) in which *P. argentipes*, which had just emerged from their pupal cases, were marked, released, and then looked for on successive days. Smith was convinced that the marked flies, which were released in places where *argentipes* were breeding in nature, did not migrate to any extent. In their first experiment, in which marking was done by the dusting of fluorescein or the removal of one middle leg, it was believed that 2 out of a total of 667 flies had been recovered on the 15th day after release. We pointed out that identification of so delicate an insect by means of a missing leg was obviously open to fallacy and that this finding could not therefore be accepted as genuine. We strengthened our arguments by pointing out that in all subsequent experiments of this type, Smith abandoned this unreliable method of marking, and that after a reliable method had been substituted for it, not a single fly was re-captured after the sixth day out of 3,271 plus 428 flies released. Malone in his 'Rejoinder' mentions yet another experiment of this type in which, again, not one fly out of 810 released was re-captured after the fifth day. In all, therefore, we have 4,509 properly marked flies released in these experiments, of which not a fly was re-captured after the sixth day, and of those recovered only three were found as late as the sixth day. We claimed that this indicated that *P. argentipes* in nature rarely lived as long as six days, and never longer, and that this was confirmed by Christophers, Shortt and Barraud (1926) who stated with regard to laboratory-bred flies: 'We have paid considerable attention to making conditions as favourable as possible to the flies, and have tried open nets and large and small confined spaces, with various devices and under various conditions of temperature, but without being able to prolong life beyond the periods noted (5-6 days).' Shortt in his reply states: 'In their comments it has suited the authors to ignore the previous experiment of Smith *et al.* (*loc. cit.*) where out of a much smaller number (667) recoveries of marked flies were made up to the 15th day. Our knowledge of the physiology of the sandfly makes it certain that such flies must have fed a minimum of three times to have lived so long.' Malone comments: 'This statement is incorrect, it is misleading, and it begs the question.' Malone then shows that the experiment was not ignored by us, but cited and fully commented on: that the statement is misleading.

in that supposed re-captures of flies were not made up to the 15th day but only on the 3rd, 4th, 7th and 15th days (none were recovered on the first and second days and on the intervening days not mentioned). In the subsequent experiments, after a reliable method of identification had been adopted, recoveries were made 'regularly', i.e. in decreasing numbers, everyday from the first to the sixth days (as could be expected in well-conducted experimental and not afterwards. Malone objects to Shortt's assumption that the two flies thought to have been recovered on the 15th day in this first, obviously imperfect, experiment, were genuine marked flies, and also, to his further assumption that this (supposed) finding (which certainly requires proof) shows that flies in nature may feed as often as three times. Malone states: 'This is simply begging the question and should, on no account, be taken as evidence that the sandfly feeds on more than one occasion in nature.'

II. We pointed out that Shortt *et al.* (*loc. cit.*) had observed that the male sandfly lived, as a rule, only a few hours, and that it died immediately after fertilizing one female, having in the act of fertilization 'paid its full debt to nature'. We therefore thought it unlikely that the female fly normally lived 10 days or more (if less, it cannot prove infective) and suggested that the female also probably 'paid its full debt to nature' by dying immediately after ovipositing. We stated that this probability was supported by the repeated observations of Christophers (1926) that 'the outstanding difficulty was the fact that *P. argentipes* invariably dies by the fifth day' (in the act of ovipositing or immediately afterwards) and also that a caught gravid fly, i.e. one that had had a previous blood meal, was never known to take a second blood meal when given a chance to do so in the laboratory. We remarked, moreover, that if the female fly had a span of life considerably longer than that of the male, then catches of flies should show a distinct preponderance of females, and that such a preponderance had never been noted in India, though the reverse (more males than females) was not an unusual finding. Shortt, in reply to these arguments, maintains that the mere fact that the female fly is equipped by nature with a spermatheca is conclusive evidence that it is intended to lay more than one batch of eggs, and affirms that this single fact is sufficient in itself 'completely to demolish the structure of their argument'. Malone points out that this argument, based entirely on teleological grounds, is fallacious. Thus, there is a species of moth (having a spermatheca) the normal life-span of which is one night only: a species of locust (which has a spermatheca) which lays only one batch of eggs; and a species of *Drosophila* (which has a spermatheca) which lays a single batch of eggs and dies immediately. This behaviour is exactly the same as was noted in the case of *P. argentipes* kept under natural conditions. Later, when the flies were kept at a rigidly maintained temperature of $28^{\circ}\text{C} \pm 1^{\circ}\text{C}$, and in the absence of larval food on which to lay their eggs, life of the insects was prolonged to beyond 10 days, but such devices are laboratory 'tricks of the trade' deliberately introduced for the artificial prolongation of the life of insects in captivity: they do not normally occur in nature. It is worth noting that daily variations in temperature in Assam (5°C .) even when temperatures are least variable, are much greater than laboratory-kept *P. argentipes* can withstand. Shortt, while admitting this, maintains that the sandflies return, immediately after feeding, to cracks and crannies in walls, in which he claims, temperatures remain much more uniform. Against this explanation is the fact, that to become infective, the sandflies must feed on plant juices (see under) and that these plants will naturally be growing outside human habitations. From a consideration of the points so far discussed it will be evident that *P. argentipes*, in nature, do not normally live longer than 6 or at the very most 7 days. Since it was impossible to transmit kala-azar

experimentally with flies less than 10 days old, the experiments must be regarded as representing artificial, and not natural conditions, on these grounds alone.

III. We stated that *P. argentipes* were almost certainly pure blood feeders, and quoted Napier and Smith (1926): 'The adult female sucks blood and is a pure blood feeder' and 'The normal life-cycle of this fly appears to include only one blood meal'. (In view of the latter observation it is somewhat surprising that this line of investigation was pursued further.) We emphasized that no fresh evidence had been produced, since Napier and Smith had made the above quoted statements, to show that *P. argentipes* ever fed on plant juices, in nature, and that it had been conclusively proved that without such a diet *P. argentipes* were quite incapable of transmitting kala-azar experimentally. We maintained that the successful experiments did not represent natural conditions, in this important respect, and could not therefore be interpreted as proof that *P. argentipes*, in nature, ever transmitted kala-azar. Shortt argues that in keeping mosquitoes for experimental purposes the feeding on raisins, or other plant juices, is a normal procedure, and that it was, therefore, perfectly justifiable to give a raisin diet to the sandflies used in the successful experiments. At the same time Shortt admits that the raisin diet was unnatural and himself states that this is clearly shown by the fact that the ovaries of flies so fed fail to develop. Nevertheless, Shortt states: 'We are unaware why the writers take such exception to the feeding of sandflies on raisins and infer that this should nullify the results obtained thereby, viz, the production of successful transmission to man by the bites of flies so fed.' This inability to see the point of our argument does not agree with two statements made by Shortt: Of *P. argentipes* not given the raisin diet he states, 'Eleven human volunteers were fed upon 11,537 times by sandflies, which had previously been fed on kala-azar cases and re-fed two or more times to allow the infection fully to develop. These human experiments were entirely negative in spite of an intensity of feeding much greater than would ever occur in nature', and in the same article: 'It is difficult to get away from the supposition that the (successful) result was due to feeding on raisins (Shortt, 1945).' Mosquitoes do not require a diet of plant juice to become capable vectors of malaria.

IV. We pointed out how erroneous was the general belief that the distribution of *P. argentipes* 'coincided' with that of kala-azar in India. Shortt denies knowledge of the existence of such a belief, but Malone, quoting from the published writings of Knowles, Napier, Smith, Christophers and Shortt, shows how all these members of the Kala-azar Commission declared, at one time or another, that the distribution of the two 'coincided very close' or 'corresponded closely' or were 'apparently identical' and based their statements on Sinton's alleged observation made in 1922. After our criticism had appeared Shortt toned down his own previous remarks that Sinton had pointed out that the distribution of these two 'corresponded closely' to the following, 'Although the actual record appears to be lost, there is no doubt that in 1932 Sinton, in a private communication to Knowles, pointed out that there appeared to be some correlation between the distribution of kala-azar in India and that of *Phlebotomus argentipes*'. I stress this as yet another example of how any evidence which could possibly be interpreted as lending support to the favoured sandfly theory has been exaggerated. How small the 'correlation' was in 1922, is shown by the fact that at that time *P. argentipes* had not been found in Madras (where Patton had repeatedly looked for it), that it was unknown in the endemic centres of Kayalpatnam, and the heavily-infected islands lying between India and Ceylon, and had not even been found in Assam! Shortt now states: 'It would be more accurate to say that the distribution of

P. argentipes includes all areas in India where kala-azar is found.' The correctness of this statement is not questioned for the simple reason, previously pointed out by us, that *P. argentipes* can probably be found anywhere in India (even up to a height of 4,000 feet) if looked for sufficiently diligently. Up till now, however, the practice has been to search most carefully for *P. argentipes* only in areas from which cases of kala-azar have been reported and not to bother to look for it elsewhere, even though casual, as opposed to systematic search, has revealed the presence of the insect in many places where indigenous kala-azar is unknown. Most noteworthy of such places is Ceylon where *argentipes* has been found all over, even up to a height of 1,500 feet, where kala-azar has been repeatedly introduced by infected imported Indian coolies (Turkhud *et al.*, 1926), but where, nevertheless, kala-azar has never spread to the indigenous population. The most likely explanation for this failure of the disease to spread in Ceylon is that the people of that island will not mix, to any extent, with imported Indian coolies.

V. We pointed out that the finding of *P. argentipes* with infections of *L. donovani*, in nature, was remarkably rare, and quoted Smith who remarked that such flies were quite out of proportion to the incidence of the disease in endemic areas. We stressed the importance of the observation that not a single fly had ever been found in India with a pharynx infection, a finding which would have denoted that the fly was at least 5 or 6 days old. (In this we were mistaken for one such fly with a pharynx infection has been found.) Shortt rightly refutes our somewhat exaggerated statement that no such fly had been found 'in 20 years of unremitting research' by pointing out that search for infected flies was not unremitting for that period, and he adds: 'In all, the number found infected in nature could probably be counted on the fingers of both hands . . . it is not surprising, therefore, that no case of infection of the pharynx was found in any of the few flies caught in nature.' I have no desire to win mere debating points, but it is necessary for the reader fully to appreciate how evidence supporting the sandfly theory has been exaggerated in the past, I therefore again quote from Malone: 'Here are three quotations taken from the published writings of members of the Kala-azar Commission. 1. "At the same time it will be evident that a certain percentage of infected flies must always be present in houses harbouring kala-azar cases." 2. The occurrence in nature of *P. argentipes* infected with *L. donovani*—"This was demonstrated by the Commission with no special difficulty. Out of 345 *P. argentipes* caught in kala-azar houses 8 were found to be infected with *L. donovani*." 3. "A large percentage of flies that feed on an infected person acquire the infection: infected flies have been found repeatedly in nature." Now, however, Shortt says that such flies can probably be counted 'on the fingers of both hands', and of these extremely few flies, out of thousands of *P. argentipes* caught and examined, no less than 6 of the positive flies belonged to a batch of 69 caught in a cattle-shed. Napier and Smith (1926a) state: 'Large numbers of *P. argentipes* have been found in one cowshed adjoining a house without any being found in the house itself' and according to Knowles (1928) 'Lloyd and Napier have shown that *P. argentipes* would feed by preference, every time, on bovine blood' (i.e. in preference to human blood). Even admitting exaggeration in these statement the finding of 6 positive flies in a cattle-shed (in the small batch of 69 flies examined) can only be described as miraculous if derived from a human source. Alternatively, it suggests that these 6 flies were not infected with *L. donovani* at all, as the sandflies, preferring bovine blood, did not feed on a human being suffering from kala-azar. This reasonable alternative then throws doubt on the authenticity of the flagellates described as *L. donovani* in the remaining 2 or 3 infected flies found.

VI. We quoted at length from McCombie Young's book on kala-azar in Assam to show that the disease was almost three times as common in males as in females, and showed that other workers—Brahmachari, Korke, Michael, Acton and Napier—had all reported observations similar to those of McCombie Young's. This observation is obviously at variance with the theory that kala-azar is transmitted by a house dwelling insect. Shortt refuses to discuss the point, as, according to him, the evidence is too involved. Here is an example of how evidence conflicting with the sandfly theory is neglected, minimized or overlooked. Napier's explanation, that sandflies dislike smoke and that women suffer less from kala-azar because they sleep inside smokey huts while their husbands prefer to sleep in the cooler verandahs, is far-fetched in the extreme. Huts are seldom equipped with verandahs anywhere, and in rainy Assam it is unlikely that men will sleep out of doors, during the monsoon months, the season when infection is most commonly acquired.

It will be seen that in reality, there is little good evidence which even suggests that *P. argentipes* is the probable vector of kala-azar. Admittedly, successful transmission has been attained with these insects but only under highly artificial conditions, and such purely 'laboratory' results are well known in connection with other diseases which can be experimentally transmitted by insects which normally play no part in the dissemination of them. Indeed, it is likely that bed bugs could be made to transmit syphilis under conditions less artificial than those used in the successful kala-azar experiments, but even if this were proved we would still continue to attribute syphilis to contact. Rogers (1914) noted that European planters who had sexual intercourse with infected women acquired kala-azar, but here, instead of admitting that contact caused the infection, *P. argentipes* are dragged in and blamed because they can be experimentally induced to transmit this disease.

Consider now further evidence not discussed in the three papers on which arguments have hitherto been based.

Napier and Smith (*loc. cit.*) state: '*P. argentipes* have a very limited flight . . . they have never been found in unused rooms or far from their food supply. . . . In one house they have been repeatedly observed in one room in which they were actually breeding but they were never observed in the adjoining room which was also used as a sleeping quarter.' All these observations completely fit the theory that kala-azar is carried by an insect which has a very limited range of flight, so limited in fact, that it cannot possibly cause epidemics in crowded Calcutta, where kala-azar therefore remains endemic—but, according to Christophers (1926a) 'The villages of Assam consist for the most part of isolated homesteads from 50 to 100 yards or more apart', and in Assam we have devastating epidemics of kala-azar. Next, in writing of laboratory-kept sandflies Adler and Theodor (1926) stress the great importance of care with regard to the cotton-wool plugs of test-tubes in which the flies are kept in laboratories. They state: 'The wool must be moistened daily but no fluid must be allowed to enter the tube, for if the wings of *P. papatasi* are even slightly moistened the insects adhere to the sides of the tube and die', and Whittingham and Rook (1923) state: 'Adults (*P. papatasi*) dislike damp and instinctively avoid a skin wet with perspiration'. (*P. papatasi* is a more robust insect than *P. argentipes*.) Reconcile these observations with the fact that kala-azar is most prevalent in Assam which is one of the wettest places in the world: that infection is invariably acquired during the monsoon months, at a time when skins are pouring with perspiration: that to become infective these delicate insects, which cannot withstand a variation of more than 2°C. under the most favourable of laboratory conditions and which dislike damp, defy weather conditions: that they leave the room

in which they have had their first blood meal on a kala-azar patient: that they seek an unnatural diet of hypothetical plant juices—a diet which prevents the development of their ovaries and 'blocks' them—and that in this enfeebled state, they either return to the house, or else proceed 50 to 100 yards or more to another house where they carefully select their next victim, not less than 2 years of age, but one who is a male in preference to a house dwelling female.

The epidemiology of kala-azar has been built up on the assumption that the disease is transmitted by an insect which has a very limited range of flight. Such an epidemiology must necessarily bear some resemblance to one which suggests that infection is acquired through contact. Many workers have stressed the importance of contact—notably Rogers, Korke and Michael. Christophers (1926b) noted that whilst feeding sandflies members of the Commission spent many occasions, both by day and night, sitting or reclining on the mud floors of kala-azar huts but never had occasion to repent of their rashness in so doing and this also suggests that close contact, and not *argentipes*, is the important factor. Elsewhere I have shown that there are good reasons for regarding kala-azar as essentially a skin disease (Brooks, 1949). Leprosy is a 'contact' disease, and points of resemblance between leprosy and kala-azar are too striking to be merely due to coincidence. Thus the age incidence of two diseases (making due allowance for the longer incubation of leprosy) is identical. The sex distribution about three males to one female is the same in both diseases. House and household infections are marked characteristics common to both diseases. Generally speaking, prolonged contact appears necessary for the establishment of both diseases. (Thus Price, 1923, noted that in epidemics it was the old coolies 'old by length of residence not in years' who were the principal sufferers. Incidentally, the same writer—Price, 1933—states 'that the sandfly theory of transmission has not been proved is not surprising. In the light of many years' clinical experience of kala-azar I fail to see how the sandfly can possibly be implicated'). In both diseases the parasite is in the skin but during fever may be found in the blood stream (in kala-azar the parasite in the blood is phagocytosed and the blood cannot therefore be regarded as the natural habitat of the parasite). The second stage of dermal leishmanoid often bears so striking a resemblance to leprosy that, clinically, it may be indistinguishable from that disease. It has been claimed that the same experimental animal—the Syrian hamster—may be infected with both diseases, and also that the parasites of both diseases will grow together in symbiosis (Row, 1946). Last it be argued that kala-azar has too limited a distribution to be a contact disease may I remind readers that Yaws has a still more limited geographical distribution.

One way of silencing a criticism is to ignore it. This method appears to have been adopted by those who may well hope that our brief criticisms, published so far in the one journal only, will be overlooked. Malone's 'Rejoinder' has not yet received the courtesy of a review in the 'Tropical Diseases Bulletin'. It may be hoped by some, that their silence will be interpreted as indicating that the favoured theory is so firmly established that it needs no defence against our worthless criticism. This easy avenue of escape from an untenable position is no longer open to them for I give below extracts from a letter written to me by the eminent Protozoologist, Dr. Clifford Dobell, F.R.S., of the National Institute for Medical Research, London: I have just seen your article on 'Leishmaniasis and the Sandfly' published in the May number of the *I.M.G.* (84, 224). Your criticism

seems to me to be fully justified and I am in complete agreement with your conclusions. From a scientific and logical standpoint there is no good evidence to convict the sandfly: and when one takes into consideration the enormous number of carefully conducted negative experiments which have been made with these insects, the verdict should surely be 'not proven' or even, perhaps, 'not guilty'. Whatever the final verdict may be, I feel sure you are right in maintaining that present-day beliefs about the transmission by sandflies are not truths to be taught in textbooks but classical examples of 'wishful thinking'. . . . I congratulate you on your stand against what is at present little more than a protozoological myth.

Iu very kindly giving me permission to quote from his letter Dr. Dobell writes: 'You may quote anything you like out of my letter, as it was my considered opinion and I am ready to substantiate it. . . . Truth is the only thing that matters, so go on'. I take this opportunity of thanking Dr. Dobell for his encouragement.

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Yours faithfully,
A. G. BROOKS,
Assistant Surgeon, I.M.D.

CENTRAL RESEARCH INSTITUTE,
KASALI,
6th December, 1949.

[After the publication of Malone's rejoinder, *I.M.G.*, 1947, 82, p. 544, many readers asked for a considered opinion on the rôle of the sandfly in kala-azar. The re-opening of the controversy with this letter, it is hoped, will provide the desired opinion from the workers and readers themselves. The case against the sandfly may still be 'not proven'.—EDITOR, *I.M.G.*]

AUREOMYCIN IN KALA-AZAR

To the Editor, '*Indian Medical Gazette*'

SIR,—We have recently tried aureomycin in the treatment of kala-azar. This antibiotic drug is effective against many of the Gram-positive and Gram-negative organisms and is highly specific against rickettsial organisms. It is also effective against several viral infections. In view of the fact that aureomycin is effective against rickettsial organisms that are intracellular parasites, it seemed worthwhile to test if this drug had any effect on *Leishmania donovani* that is also an intracellular parasite in man.

The drug was used for the treatment of three cases of kala-azar under the care of one of us (P. C. S. G.).

Case 1.—A female child, aged 10 years, suffering from kala-azar for about three months; spleen enlarged to 2½ inches below costal margin; aldehyde test + + +, complement-fixation test for kala-azar 'positive'. L-D. bodies present in ileum puncture smear, hæmoglobin 7.15 gm. per 100 ml., RBC 2.89 million, WBC 3.55 thousand per c.mm., weight 35 lb. Given aureomycin 0.5 gm. every six hours for four days and 0.25 gm. six hourly for the next six days; total 14 gm. in ten days. The fever came down on the fifth day but recurred from the eighth day. There was no improvement in the blood count, size of the spleen or fever after the course of treatment.

Case 2.—A male child, aged 7 years, suffering from kala-azar for about 4 months. Spleen 4½ inches below the costal margin, liver enlarged. Aldehyde test + + +, complement-fixation test for kala-azar 'positive'. *Leishmania donovani* present in ileum puncture smear. Hæmoglobin 6.45 gm. per cent. RBC 2.04 million and WBC 4.0 thousand per c.mm. Aureomycin 0.5 gm. six hourly for four days followed by 0.25 gm. six hourly for six days. The fever came down to some extent about the fifth day but it recurred soon after. The splenic enlargement persisted but the hepatic enlargement appeared to be slightly less. Blood count did not show any improvement. The weight was maintained at 45 lb.

Case 3.—A male patient, aged 49 years, suffering from kala-azar for about two months. Spleen enlarged to 4 inches, liver enlarged, weight 94 lb. Aldehyde test negative, complement-fixation test for kala-azar 'positive'. *Leishmania donovani* present in sternal puncture smear. Hæmoglobin 6.875 gm. per cent. RBC 2.46 million and WBC 3.3 thousand per c.mm. Aureomycin was administered in 0.5 gm. doses every six hours for ten days, total dose 20 gm. The patient who was having low pyrexia did not show any variation in the range of temperature at the end of the course of treatment and there was no change in the size of

the spleen, blood picture and body weight. Only an amœbic ulceration of the lower bowel showed signs of healing on sigmoidoscopic examination, at the end of the course of treatment with aureomycin.

Except for marked asthenia about the fourth day of the course of treatment with aureomycin in the two children no other untoward reactions were noted.

It will be apparent from the notes of the three cases that aureomycin has little action in kala-azar.

Yours faithfully,
J. C. GUPTA,
Director, School of Tropical Medicine

P. C. SEN GUPTA,
Officer-in-charge, Kala-azar Research Department

17th July, 1950.

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CONTENTS

Page

ORIGINAL ARTICLES

- Metaphysial Aclasis.** By J. N. Berry.
M.D., M.R.C.P., D.C.H. (Lond.) .. 387

- Urinary Excretion of Antimony after Administration of Methyl Glucamine Antimoniate. Preliminary observations.** By R. N. Chakravarti, D.Sc., and P. C. Sen Gupta, M.B. .. 388

- Muscular Anomalies.** By Balbir Singh, P.C.M.S., and Harish Khanna .. 391

- Studies on Plasma Protein. II. Amœbic dysentery and liver disease.** By H. Chakravarti, M.D. (Cal.) .. 394

- Chloromycetin in the Treatment of Cholera.** By R. N. Chaudhuri, S. Ghosal and M. N. Rai Chaudhuri .. 398

- A Rapid Method of Iron Hæmatoxylin Stain for Protozoa in Tissue Sections and Smears.** By P. C. Sen Gupta, M.B., K. C. Basu Mallick, M.B., and B. Bhattacharya, M.B. .. 400

A MIRROR OF HOSPITAL PRACTICE

- A Case of Hydronephrotic Kidney.** By K. G. Solanki, L.M.P. (Bom.) .. 402

- A Case of Cerebral Malaria.** By K. D. Jain, M.B., B.S. .. 403

- Uterine Manifestations of Vitamin-B Deficiency.** By M. S. Wagle, L.M.S. 404

EDITORIAL

- Atom Bomb Made Easy** .. 405

MEDICAL NEWS

- NOTIFICATION** .. 406

- QUARANTINE RESTRICTIONS** .. 406

- THE SECOND ANNUAL ALL-INDIA CONFERENCE OF INDUSTRIAL MEDICINE (17TH, 18TH AND 19TH DECEMBER, 1950, AT JAMSHEDPUR)** .. 406

- THE TUBERCULOSIS PROBLEM IN INDIA: TUBERCULOSIS SEALS SALE** .. 407

Page

- SMALLPOX VACCINE** .. 409

- DRUG FOR LEPROSY IN FAKFAK** .. 409

- TYPHUS VACCINE FOR AFGHANISTAN** .. 409

- SAVE THE CHILDREN CONFERENCE** .. 410

- TELEVISION AN EYE OPERATION** .. 410

- TELEVISION EYE OPERATIONS** .. 411

- SEARCH FOR NEW SOURCE OF ANTI-ARTHRITIC DRUG.** By Trevor I. Williams 411

- 27TH ALL-INDIA MEDICAL CONFERENCE** .. 411

PUBLIC HEALTH SECTION

- Biometric Studies of School Children of Hyderabad State.** By M. B. Daver 412

- A Field Investigation into Lathyrism.** By M. N. Rudra and L. Kant .. 415

- The Risk of Pollution of Ground Water from Borehole Latrines.** By K. Subrahmanyam and T. R. Bhaskaran 418

FIFTY YEARS AGO

- LONDON LETTER** (*Indian Medical Gazette*, September 1900, Vol. 35, p. 360) .. 421

CURRENT TOPICS, ETC.

- METEORITES BRING NEWS FROM SPACE.** By Maurice Goldsmith (UNESCO Features, No. 27, 15th August, 1950, p. 12) .. 422

- NUTRITIONAL MEGALOBlastic ANÆMIA: SO-CALLED PERNICIOUS ANÆMIA OF PREGNANCY.** By B. V. Kothari and Y. M. Bhende (*Indian Journal of Medical Research*, Vol. 37, July 1949, p. 347) .. 422

- TREATMENT OF TYPHOID FEVER WITH BACTERIOPHAGE.** By R. G. Dhayagude and D. D. Banker (*Indian Journal of Medical Research*, Vol. 37, July 1949, p. 249) .. 423

- PENICILLIN AND BLACK HAIRY TONGUE.** By W. E. Overman (*Journal of the American Medical Association*, Vol. 141, 31st December, 1949, p. 1319) .. 423

(Continued on page 386)

CONTENTS—(Continued from page 385)

	Page		Page
AIR-COOLED BUILDINGS AND ELECTRIC FANS (<i>Journal of the American Medical Association</i> , Vol. 141, 31st December, 1949, p. 1329)	423	EPILEPSY AS A SEQUELA OF RECURRENT MALARIA	428
EXTRACT OF WINGS OF PHILIPPINE BUTTER- FLY, <i>Terias hecabe</i> LINNAEUS, NEW ANTIBIOTIC FOR MALARIA. By E. Y. Garcia (<i>Philippine Medical Association Journal</i> , Vol. 25, June 1949, p. 279, as abstracted in the <i>Journal of the American Medical Association</i> , Vol. 142, 7th January, 1950, p. 63)	423	THE METABOLIC FATE OF THE INFUSED ERYTHROCYTE	429
PERTUSSIS TREATED WITH CHLORAM- PHENICOL. By E. H. Payne et al. (<i>Journal of the American Medical Asso- ciation</i> , Vol. 141, 31st December, 1949, p. 1298)	424	ERRATUM	429
CONTROL OF BIOLOGICAL WARFARE (<i>British Medical Journal</i> , i, 14th January, 1950, p. 112)	424	REVIEWS	
CYPRUS FREED FROM MALARIA. SUCCESSFUL CAMPAIGN (<i>British Medical Journal</i> , i, 14th January, 1950, p. 119)	424	THE COMMON DISEASES OF THE SKIN : A HANDBOOK FOR THE STUDENTS AND MEDICAL PRACTITIONERS. By R. Cranston Low, M.D., F.R.C.P.E., F.R.S.E., and G. A. Grant Peterkin, M.B.E., M.B., F.R.C.P. (Edin.). Fourth Edition. 1949	429
RECENT ADVANCES IN THE STUDY OF VENEREAL DISEASE. By J. E. Moore (<i>Proceedings of the Royal Society of Medicine</i> , Vol. 42, August 1949, p. 629)	425	HAPPY TOIL : FIFTY-FIVE YEARS OF TROPICAL MEDICINE. By Sir Leonard Rogers, K.C.S.I., C.I.E., F.R.C.P., F.R.C.S., LL.D., F.R.S. 1950	430
THE MANAGEMENT OF ACNE IN GENERAL PRACTICE. By H. W. Jolly and M. E. Kopfler (<i>New Orleans Medical and Surgical Journal</i> , Vol. 102, December 1949, p. 312)	425	HANDBOOK OF OBSTETRICS AND DIAGNOSTIC GYNAECOLOGY. By Leo Doyle, M.D., M.S. First Edition. 1950	430
RELIEF OF TOOTHACHE (<i>Practitioner</i> , Vol. 163, November 1949, p. 476)	426	APPLIED MEDICINE. By G. E. Beaumont, M.A., D.M., F.R.C.P., D.P.H. 1950	430
GAMMEXANE IN THE TREATMENT OF HEAD LICE (<i>Practitioner</i> , Vol. 163, November 1949, p. 475)	426	CURRENT THERAPY, 1950. LATEST AP- PROVED METHODS OF TREATMENT FOR THE PRACTISING PHYSICIAN. By Howard F. Cohn, M.D., and Twelve Consulting Editors	431
SODIUM PROPIONATE IN THE TREATMENT OF PRURITUS VULVAE (<i>Practitioner</i> , Vol. 163, November 1949, p. 475)	427	A TWENTIETH CENTURY PHYSICIAN : BEING THE REMINISCENCES OF SIR ARTHUR HURST, D.M., F.R.C.P. With a Fore- word by Professor John A. Ryle, M.D., F.R.C.P.	431
EARLY AND DELAYED CLINICAL EFFECTS OF VAGOTOMY FOR PEPTIC ULCER	427	BOOK NOTICE	432
RELIEF OF CHRONIC HYPERTENSION BY EXCISION OF PHEOCHROMOCYTOMA	428	ABSTRACTS FROM REPORTS	
SURGICAL TREATMENT OF ELEPHANTIASIS OF THE LOWER EXTREMITIES	428	REPORT OF THE SCIENTIFIC ADVISORY BOARD, IRFA, FOR THE YEAR 1949	432
THE CLINICAL EVALUATION OF AUREOMYCIN	428	CORRESPONDENCE	
		GENERALIZED CYSTICERCOSIS CELLULOSA	433
		PALUDRINE POISONING	433
		ADVERTISEMENTS IN MEDICAL JOURNALS	434
		ANY QUESTIONS	
		OPHTHALMOLOGICAL JOURNALS	434
		TREATMENT OF THREAD-WORMS	434

Original Articles

METAPHYSIAL ACLASIS

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METAPHYSIAL aclasis is a developmental disorder of the bones in which there are cancellous bony exostoses along with varying degrees of failure of remodelling or tubulation of the metaphysis by the subperiosteal osteoclastic tissue.

The bony exostoses arise from islets of cartilage left behind from the epiphysal plate. The cancellous exostoses, capped with cartilage, appear early in life and keep on growing as long as the parent epiphysal cartilage is adding to the length of the bone, hence increase in their size goes on till puberty and will stop last at the growing end of the bone, where they are also most numerous.

The bones chiefly affected are the long bones which are developed both in cartilage and membrane. The distal end of femur, the proximal ends of tibia and fibula, the proximal end of humerus, the distal ends of radius and ulna are the usual sites. The iliac crests, the vertebral borders of scapulae, the clavicles, the ribs, the metacarpal and phalangeal bones and spinal neural arches are less commonly involved. The epiphyses are always spared.

The first case was described in 1825 in the *Lancet* in the Guy's Hospital report and later on the condition was described by Ceaser Hawkins in 1837 as laminated exostosis (quoted by Bick, 1948). Ollier (1898) first gave the name of multiple exostoses and two years later discussed it under the name of dyschondroplasia (Ollier, 1900). Ehrenfried (1917), while reviewing the literature of more than 600 cases then, gave it the name hereditary deforming chondrodysplasia but also included multiple chondromata under the same heading. Keith (1920) gave it the modern name of diaphysal aclasis which was later improved upon by Greig (1931) to metaphysal aclasis. Fairbanks (1949) has recently summarized our knowledge about the disease and published five of his own cases under the name of diaphysal aclasis.

Some workers, Hunter and Wiles (1935) and Hunter (1946), consider this condition of multiple exostoses or diaphysal or metaphysal aclasis as one variety of dyschondroplasia, while others, Brailsford (1948) and Fairbanks (1949), limit the later term to the cases where the cartilaginous rests remain endosteal and consider those cases where these rests give rise to bony outgrowths on the surface of the parent bone (metaphysal aclasis) as a separate entity.

A case of metaphysal aclasis that was seen recently in this hospital is being described here.

Case report

M. R., 7 years old, male child, admitted on 17th December, 1949, with the complaints that for the last 2½ years he has had swellings on the legs which are painful and which do not permit him to bend his knees fully and that for the same period he has been getting pain in the legs on changing sides in bed. The swellings were first noticed two and a half years ago and have since been increasing in size. There was nothing relevant in the past history.

Family history.—Parents and one elder sister alive and healthy, one brother and two sisters dead due to causes irrelevant to the present condition. The father was later on examined clinically and radiologically but did not show any exostosis. The child developed normally and like other children of his age he goes to the school.

Physical examination.—A well-built, active, fairly well-developed child, normal intelligence, height 42½ inches, weight 35 lb., skull circumference 19½ inches. Temperature 98.6°F. Pulse 96. Respiration 20. There was no unilateral shortening of one limb and apart from the bony swellings and the limitation of joint movement therefrom, as described below, there was no other abnormality (figures 1 and 2, plate XLIV).

Right arm.—Small bony protuberance on medial side of the arm and another on the anteromedial surface near the upper end of humerus. Right shoulder movements full.

Tip of the styloid process one inch above the lower end of the styloid process of the radius. Ulnar deviation of the hand possible to right angle.

Small bony exostosis at the base of second phalanx right middle finger and slight ulnar deviation at the proximal interphalangeal joint of the same finger. Another exostosis at the base of second phalanx third finger which is bent slightly laterally at the proximal interphalangeal joint. Movements full.

Left arm.—One exostosis on the medial and another on the lateral surface of humerus near the insertion of deltoid, both larger than that on the right.

A small exostosis near the lower end of the left ulna. The styloid process of the ulna half an inch above the radial styloid process. Movements up to 120 degrees at the wrist joint, medially.

Right leg.—Bony protuberances round the knee joints, one on the anteromedial surface of the knee projecting upwards from the femur, another small one in popliteal fossa from the posterior surface of the lower end of femur and yet another large, nodular sessile exostosis at the head of fibula. Right knee cannot be flexed beyond 60 degrees and full flexion was painful.

Left leg.—Two adjacent sessile exostoses just above the knee from the medial surface of femur and one large bony swelling in the popliteal fossa tender on pressure. Flexion in the left knee possible up to 50 degrees.

One small sessile exostosis two inches above the left ankle between tibia and fibula anteriorly on lateral side of shin and another small one just above the medial malleolus.

No other exostosis palpable.

All the exostoses which are of any size point towards the middle of the shaft leading to a concavity on that side and a gradual sloping surface towards the epiphysial end. The only exception is the one at the upper end of right fibula which is large, sessile and has an irregular surface.

Other exostoses.—Skiagrams show multiple cancellous exostoses (figure 3, plate XLIV and figures 4, 5 and 6, plate XLV) continuous with the shaft of the bones. Right ulna is shorter than the corresponding bone of the opposite side. The necks of both the femora show absence of remodelling. For biopsy, material from the exostosis at the head of the right fibula was taken. The pathologist's (Professor G. L. Sharma) report was—

Gross: One piece of biopsy tissue received. The tissue is bony, measuring 2.4 cm. \times 1.6 cm. \times 1.2 cm. Some area of sectioned surface is spongy and other area is solid.

Microscopic: The histologic characterization of the specimen consisted of well-formed numerous bony trabeculae continuous with a layer of mature hyaline cartilage cells suggesting osteogenesis from the latter cells. There are plentiful deeply stained osteoblasts abutting against the trabeculae. The marrow spaces contain nucleated cells of the erythroid and myeloid series (figure 7, plate XLV and figure 8, plate XLVI).

Pathological diagnosis: Diaphysial aklasis or chondrodysplasia.

Comments

This is a typical example of metaphysial aklasis showing both the pedunculated and sessile exostoses and also absence of remodelling of the metaphyses as shown in the necks of the femora as well as shortening of the ulna. The symptoms, e.g. hard bony swelling, pains and limitation of movements of joints, began only at the age of four and half years and as usual nothing abnormal was noticed during the infancy. The pains here were probably due to inflammation of bursae over the exostoses round about the knee joints and this subsided with rest alone. The biopsy of an exostosis showed typical cancellous bone covered with hyaline cartilage and suggesting the growth of the exostosis from the covering cartilage. The disease is often hereditary but in this case the father did not

show any exostoses. None of the sibs could be examined.

Summary

A case of metaphysial aklasis has been described in detail. The aetiology, pathology and history of the disease and its development have been described briefly.

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URINARY EXCRETION OF ANTIMONY AFTER ADMINISTRATION OF METHYL GLUCAMINE ANTIMONIATE

PRELIMINARY OBSERVATIONS

By

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METHYL glucamine antimoniate is one of the recently introduced pentavalent antimony compounds that has been found to yield satisfactory results in the treatment of kala-azar in India and the Mediterranean countries (Sen Gupta, 1950). The compound contains 28.35 per cent of antimony and the 30 per cent solution that is used for intramuscular injections contains 0.425 gm. of antimony in 5 cc. The maximum single dose for adults varies from 15 to 20 cc. according to the body weight corresponding to 1.27 to 1.6 gm. of antimony. The drug is of low toxicity and is reported to be very rapidly excreted. Durand *et al.* (1946) found that in healthy subjects the drug is almost completely excreted in the urine within 24 hours and no

traces of Sb are found after this period. In kala-azar cases traces of antimony could be detected up to 36 hours but not 12 hours later. We have studied the urinary excretion of antimony subsequent to intramuscular injection of methyl glucamine antimoniate (MGA) in three cases of kala-azar under the care of one of us (P. C. S. G.) and the results obtained are incorporated in this paper.

The diagnosis of kala-azar was confirmed in all the three cases by Napier's aldehyde test; the complement fixation test for kala-azar carried out according to the technique described by one of us (Sen Gupta, 1945) and by finding *Leishmania donovani* in the sternal puncture smear. All the three patients showed anaemia, leucopenia, hypo-albuminaemia with hyper-globulinaemia. Examination of the urine did not show any abnormality; the urea clearance test was done in cases 1 and 3 before specific treatment and case 1 showed Cm* 57 per cent and case 3 Cs* 73.9 per cent.

The patients were given single intramuscular injections of methyl glucamine antimoniate and samples of urine were collected at the end of 1 and 2 hours and the entire amounts passed till 12, 24, 36, 48, 60 and 72 hours. The amount of

antimony in each of these samples was estimated according to a method adapted from that of Macallum (1923). The details of the method followed are given below:

100 cc. sample of urine or the entire quantity, if the amount was less than 100 cc., was evaporated to 5 to 10 cc. on a steam-bath and washed out with 10 to 15 cc. of water and 25 cc. of concentrated sulphuric acid into a 250 cc. Kjeldahl flask. The flask was cooled under the tap and 6 gm. of potassium permanganate were carefully added. After the initial frothing was over, it was heated on sand-bath for an hour and cooled. 20 cc. of conc. hydrochloric acid were then slowly added and the flask again heated on sand-bath. A clear faintly yellow to colourless solution was obtained in about half an hour. The heating was continued till the vapour was free from chlorine (i.e. no blue coloration of cadmium iodide starch paper). In some of the experiments a white product crystallized out before it was possible to drive off the chlorine completely. In such cases 10 to 15 cc. of conc. HCl were added to dissolve the white product and the heating was continued till the vapour was free from chlorine. It was finally washed out with 20 cc. of conc. HCl and

TABLE I

Amount of MGA administered and date	Urine collected till hours after injection	Amount in cc.	Antimony content (gm.)	Cumulative per cent of Sb dose excreted
Case 1				
5 cc. = 0.425 gm. Sb on 1-5-1950 ..	1 hour	75	0.047	11.0
	2 hours	15	0.075	28.7
	12 hours	703	0.217	79.7
	24 hours	840	0.035	83.0
	(?) 48 hours	410	0.0	..
	(?) 72 hours	860	0.0	..
5 cc. = 0.425 gm. Sb on 10-5-1950 ..	1 hour	60	0.021	4.9
	2 hours	30	0.067	20.7
	24 hours	870	0.276	85.6
	36 hours	850	0.020	90.4
	48 hours	1,000	0.010	92.8
	60 hours	850	0.0	..
	72 hours	400	0.0	..
Case 2				
5 cc. = 0.425 gm. Sb on 5-6-1950 ..	1 hour	30	0.052	12.2
	2 hours	30	0.056	25.5
	12 hours	550	0.165	64.2
	24 hours	650	0.058	77.9
	36 hours	550	0.043	83.0
	48 hours	1,200	0.008	89.8
	60 hours	630	0.0	..
	72 hours	1,050	0.0	..
Case 3				
5 cc. = 0.425 gm. Sb on 12-6-1950 ..	1 hour	40	0.051	12.0
	2 hours	50	0.069	28.2
	12 hours	690	0.225	81.1
	24 hours	350	0.045	91.7
	36 hours	1,275	0.015	96.4
	48 hours	300	0.0	..
	60 hours	910	0.0	..
	72 hours	390	0.0	..

* Cm = maximum clearance; Cs = standard clearance.

20 cc. of water into a 500 cc. stoppered conical flask, cooled to room temperature and excess of potassium iodide (6 gm.) was added. The flask was immediately stoppered and shaken for 5 minutes. The contents of the flask were then diluted with 300 cc. of water, cooled and titrated with decinormal sodium thiosulphate solution using starch solution as indicator. One to two cc. of the starch solution were added during the later stages of titration as indicated by the disappearance of the brown tinge of the solution. The null point was indicated by the disappearance of the blue colour of iodine starch complex, the solution being faintly yellow or colourless. One cc. of N/10 sodium thiosulphate is equivalent to 0.006 gm. of antimony.

The results of estimation of antimony in the different samples of urine collected after the administration of MGA in the three patients are given in table I.

Discussion

In our study of urinary excretion of antimony after administration of methyl glucamine antimoniate, we had to employ a chemical quantitative method that was no doubt time consuming and that did not allow us to determine whether the antimony excreted was in the tri- or the pentavalent state, because a polarograph was not available. But the results obtained compare favourably with those obtained by other workers with MGA and other antimony compounds.

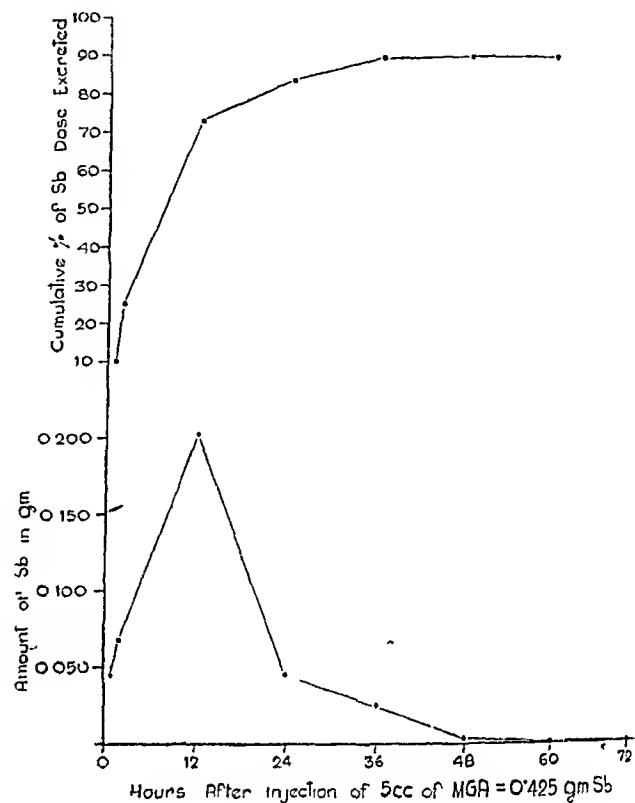
It will be seen from table I that there was a wide variation in the amount of antimony excreted during the first and the second hours following the intramuscular injection of MGA in the different experiments in the three cases. This is obviously due to the irregular absorption into the system following intramuscular injections. By twenty-four hours however it seems that the absorption is more or less complete because the amount of antimony excreted is more or less identical in the same individual.

Table II and the chart show the average values of the amount of antimony excreted and the cumulative per cent of the antimony dose following MGA.

TABLE II

Urine collected till hours after the injection of MGA = 0.425 gm Sb	Amount of antimony excreted in gm	Cumulative per cent of Sb dose excreted
1 hour	0.043	10.2
2 hours	0.067	25.8
12 hours	0.202	73.4
24 hours	0.046	84.2
36 hours	0.026	90.3
48 hours	0.0045	91.3
60 hours	0.000	..
72 hours	0.000	..

A study of the average values relating to the excretion of antimony shows that approximately one-fourth of the drug administered is excreted in two hours, about three-fourths in 12 hours and by 24 hours over 80 per cent. Small amounts of antimony are excreted up till 48 hours but not later. It appears that the excretion of antimony after intramuscular injection of MGA is somewhat similar to that following sodium antimony gluconate. A patient suffering from Mediterranean kala-azar, who had been given 100 mg. of Sb as sodium antimony gluconate, excreted 77.4 per cent of the dose of Sb in 24 hours (Goodwin and Page, 1943).



Durand *et al.* (*loc. cit.*) found that traces of antimony could be detected in the urine of kala-azar patients up to 36 hours after the administration of MGA. In our cases in two instances antimony could be detected in the urine till 48 hours. In normal human subjects the excretion of antimony ceases after 24 hours (Durand *et al.*, *loc. cit.*) but excretion is slower and continued for a longer time in kala-azar. This is probably due to the renal hypofunction seen in some cases of kala-azar (Sen Gupta *et al.*, unpublished data). In case 1, the urea clearance test showed subnormal values. In this patient and in case 2, small amounts of antimony could be detected in the urine till 48 hours and the total amount of Sb excreted in 24 hours was less than that in case 3 in which the urea clearance test showed values within normal range. In case 3 the amount of antimony excreted was also greater and no trace of antimony could be detected in the urine after 36 hours.

The fact that the urinary excretion of antimony ceases after 48 hours and over 90 per

cent of the drug administered is excreted during this period is of value in determining the safe interval between two injections of MGA a compound that is administered in a dosage containing a large amount of antimony. If the successive doses are separated by 48 hours, there seems to be little danger of cumulative toxic action. This scheme of administering MGA on alternate days does not affect its therapeutic efficiency. This will be apparent from the results of the clinical trials of this compound by one of the writers in Indian kala-azar (Sen Gupta, 1950).

Summary

Urinary excretion of antimony subsequent to intramuscular injection of methyl glucamine antimoniate was studied in three cases of Indian kala-azar. It was found that on an average approximately one-fourth of the antimony dose was excreted in 2 hours and three-fourths in 12 hours. In 48 hours approximately 90 per cent of the antimony of the dose administered was excreted in the urine. Antimony could not be detected in the urine after 48 hours.

In normal individuals excretion of antimony in the urine is completed in 24 hours after the injection of methyl glucamine antimoniate. There is thus a delay in the urinary excretion of antimony in kala-azar. In view of the presence of signs of renal hypofunction as indicated by the urea clearance test, in some cases of kala-azar, it is suggested that the delay in excretion of antimony in kala-azar cases may be due partly at least to the presence of renal hypofunction.

It appears that if the injections of this drug are given on alternate days, there is little chance of cumulative toxic action due to antimony. This is of importance on account of the high antimony content of the drug. Administration of the drug on alternate days does not affect its therapeutic efficiency.

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MUSCULAR ANOMALIES

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The Axilla

During the routine work in the Anatomy Department, Medical College, Amritsar, an abnormally placed muscular sheet, 5 inches by 1 inch, was found in both axillae of a body. It was

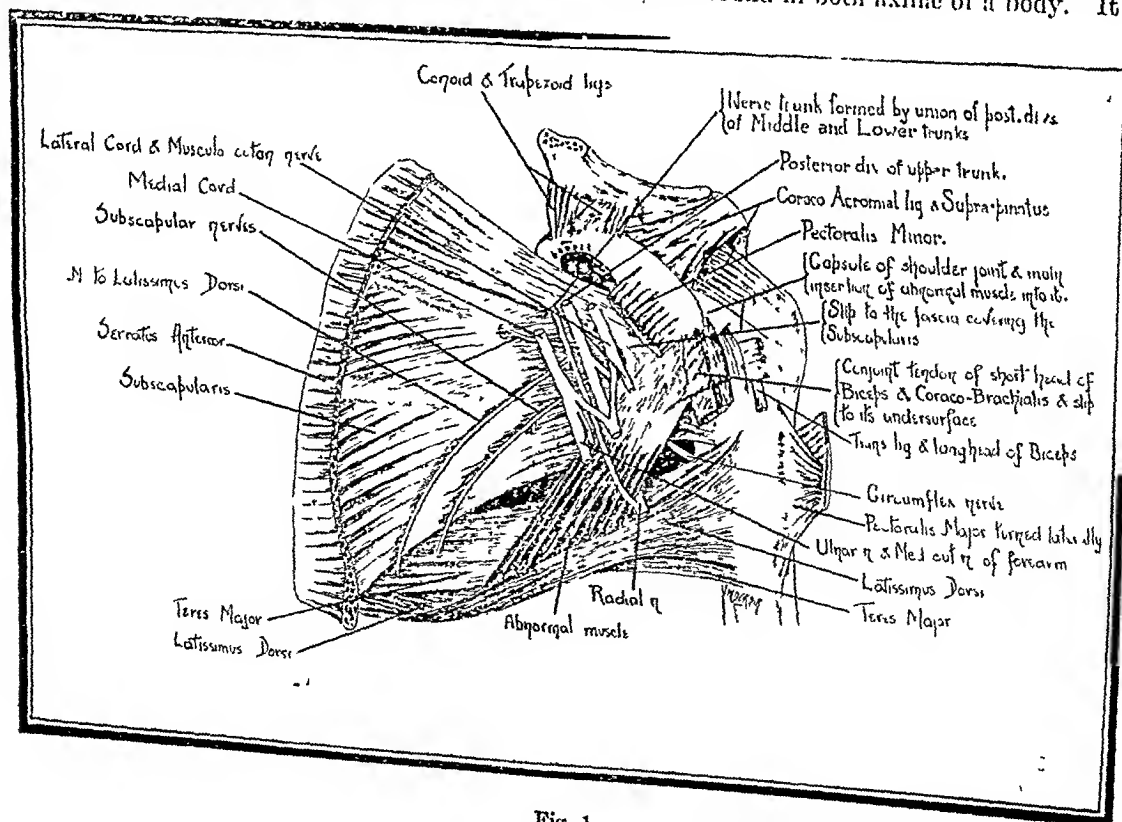


Fig. 1.

running obliquely upwards and slightly laterally from the centre of posterior axillary fold to the shoulder and was lying deep in the axilla on its posterior wall. The structures intervening were: The posterior division of upper trunk of Brachial Plexus (the usual way of formation of which was affected by this slip), the Circumflex nerve and the common trunk origin of posterior Circumflex Humeral and the Subscapular arteries which divided deep to it.

Description (Figure 1).—By its lower border which was fleshy it was attached to the centre of tendon of Latissimus Dorsi, from where it ran obliquely upward and slightly laterally applied closely to the posterior axillary wall (Teres Major and Subscapularis). An inch below the Coracoid process it became aponeurotic and here was covered by Pectoralis Minor and the conjoint tendon of origin of Coracobrachialis and short head of Biceps. Here the tendon got expanded and sent laterally and medially expansions to fuse with the under-surface of the conjoint tendon or origin of short head of Biceps and Coracobrachialis and the fascia covering Subscapularis, respectively. The main central part continued onwards deep to the Coracoid process over the upper border of Subscapularis to fuse with the top of the capsule of shoulder joint. A slender nerve from the posterior division of the upper trunk was found entering its medial border.

Relations.—Deep to the muscle were Teres Major and Subscapularis muscle. Separating it from Subscapularis were the posterior division of upper trunk, Circumflex nerve and an arterial trunk which divided deep to it into posterior Circumflex Humeral artery and the Subscapular artery. All the other nerves and vessels were superficial to it.

Effects produced on the axillary structures by its presence were: (1) The abnormal formation of Brachial Plexus. The lateral and medial cords were being formed normally but the posterior cord which is normally formed by the union of the posterior divisions of the three trunks which was not formed at all. The posterior division of upper trunk was found running down deep to this muscle and was joined by a nerve trunk resulting from the union of posterior division of middle and lower trunks (which was passing superficial to the muscle) one inch above the lower border of Teres Major to form the Radial nerve. (2) The branches of the normal posterior cord were arising in the given manner. Upper and lower Subscapular nerves and the Circumflex nerve from the posterior divisions of the upper trunk, in this order from above downwards, all arising from above the level of the muscle, and nerve to Latissimus Dorsi was arising from the nerve trunk resulting from the union of the posterior divisions of middle and lower trunk.

Discussion.—1. This muscle does not agree, both as regards its attachments and relations,

with any of the muscles described so far. The only muscle with which it tallies to some extent is the Axillary Arch found in 7 per cent of the bodies according to LeDouble. Axillary Arch stretches from the tendon of Latissimus Dorsi to the Pectoralis Major, Pectoralis Minor, Coracobrachialis, Biceps or Coracoid process. But this muscle goes even beyond the Coracoid process to the capsule of shoulder joint which the Axillary Arch nerve does.

2. It also differs from the Axillary Arch in that, while latter which is the medial thickened edge of Axillary Fascia is superficial to the main Axillary vessels and nerves, the former is lying deep in the axilla, deep to the main vessels and nerves of axilla with the exceptions already mentioned above.

3. The difficulty presented to the surgeon by the Axillary Arch in ligaturing Axillary Artery, because of its lying superficial to the usual site of ligature will not be present in this case, here the Axillary Artery is superficial to the muscle.

4. The Axillary Arch will not affect the formation of Brachial Plexus, as is being done by this muscle. In this respect the point worth noticing is about the root value of nerve to Latissimus Dorsi. Normally, the nerve to Latissimus Dorsi comes from the normal posterior cord which conveys to it fibres of the anterior primary rami of 6th, 7th and 8th Cervical nerves. But here Latissimus Dorsi muscle is being supplied by a nerve which arises from the trunk formed by the posterior divisions of middle and lower trunks. We know that the middle and lower trunks contain fibres of only 7th and 8th Cervical and 1st Thoracic and few fibres of 2nd Thoracic (which are conveyed to it by communicating twig from anterior primary ramus of 2nd Thoracic nerve). Hence from anatomical evidence given above we infer that here nerve to Latissimus Dorsi will be lacking in fibres from 6th Cervical nerve and may be containing fibres from any of the already mentioned nerves. This change of root value has a bearing on the development of the muscle, which it must have affected, i.e. the muscle must have developed from different metameres than from which it normally does.

5. It also differs from the Axillary Arch in the fact that while the latter which represents the remains of traces of Panniculus Carnosus of Lower mammals (which is normally unrepresented in man) is supplied by anterior Thoracic nerves, where this muscle is being supplied by anterior Cervical nerves as shown in figure, i.e. from Circumflex nerve, which here contains fibres of 5th, 6th and some fibres of 4th Cervical nerve.

6. That the abnormal muscular slips present in the region of the axilla present a very varied form is evident from the very sharp contrast between this slip and the modified Axillary Arch described recently by Basu (1949) of Campbell

Medical School, Calcutta, in his article 'Abnormal Pectoralis Minor muscle and evidence of modified Axillary Arch' published in the *Indian Medical Gazette* of May 1949. Whereas the slip described by Dr. Basu runs downwards from its origin to reach its insertion as low down as the medial Epicondyle of the Humerus, the muscle described here goes in the reverse direction, i.e. runs in the upward direction from its origin so as to reach the top of the capsule of the shoulder joint.

The Left Lower Limb

The left lower limb of the same body showed some muscular variations and here it were the Peronei which were affected. As usual there were two muscles attached to the lateral or the Peroneal surface of the Fibula and their attachments corresponded to the usual attachments of Peroneus Longus and Peroneus Brevis, with the difference that the one representing Peroneus Longus was very much increased in size (thickness) and the one representing the Peroneus Brevis was correspondingly very much reduced in size. So these muscles did not differ from the Peroneus Longus and Peroneus Brevis as regards their attachments to fibula, but at their lower attachments they differed from the attachments of Peroneus Longus and Peroneus Brevis a great deal and were attached in the following manner :—

(i) The tendon of the muscle representing Peroneus Brevis (P.B.) instead of passing to its usual site of insertion, i.e. the 5th Metatarsal bone, got flattened a little above the Lateral Malleolus and passing down got inserted into the Peroneal Tubercle and the lateral surface of Calcaneum behind it. The whole insertion measured one and a half inches ($1\frac{1}{2}$) in all.

(ii) The tendon of the muscle representing the Peroneus Longus (P.L.) passed as usual behind the Lateral Malleolus and then across the lateral surface of Calcaneum below and behind the Peroneal Tubercle to the commencement of the groove for Peroneus Longus on the lateral surface of Cuboid bone. A little before entering the groove it split up into two parts : a superficial and a deep, which got inserted as follows :—

The superficial part (P.L.1, figure 2) got very much flattened with its anterior and posterior parts thicker than the central portion and while the anterior and posterior parts got attached to the tuberosity on the base of 5th Metatarsal bone and the Lateral Tubercle of the Calcaneum respectively, the (central) part got fused with the top of the band of deep fascia (Lateral part of Plantar aponeurosis) running between the Lateral Tubercle of Calcaneum and the base of 5th Metatarsal bone.

The deep part (P.L.2) took the normal course and attachments of the normal tendon of Peroneus Longus.

(iii) Peroneus Tertius, except for the fact that it was very much better developed than the normal, showed no abnormality.

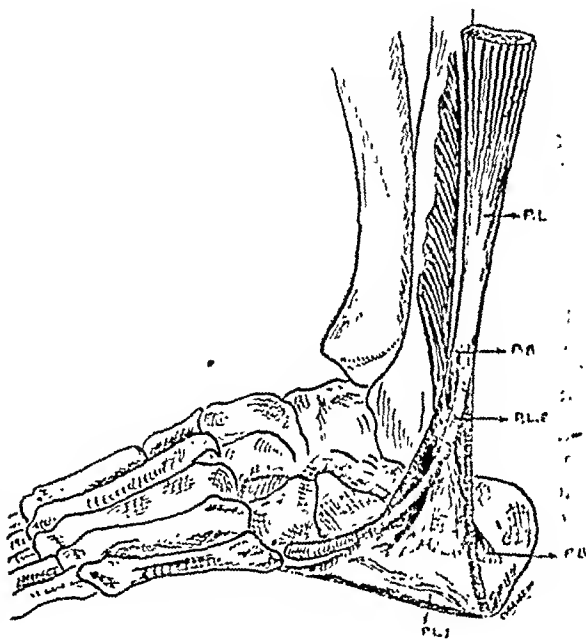


Fig. 2.

Conclusions.—From the above description of the muscles we come to the following conclusions :—

1. Peroneus Brevis is absent and is replaced by another muscle, Peroneus Digiti Quinti, found in certain monkeys in which it extends from the lower part of Fibula to the base of 5th Metatarsal bone or may be attached to the Calcaneum as in this case.
2. The loss of Peroneus Brevis, which is concerned with eversion movement of the foot, is compensated for, partly by the superficial part of tendon of Peroneus Longus (going to 5th Metatarsal) and partly by the better-developed Peroneus Tertius.
3. Presence of such structures, which represent the persisting parts of animal muscles, go a long way in favour of theory of evolution.

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STUDIES ON PLASMA PROTEIN

II. AMŒBIC DYSENTERY AND LIVER DISEASE

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In amœbic dysentery there are many factors which are well known to cause alterations in the plasma protein pattern. In the acute stage of the disease, dehydration from repeated loose stools may raise the protein level due to hæmo-concentration. Chronic amœbiasis, which is so often found amongst the teeming population, is often associated with diarrhoea; some degree of liver dysfunction is not uncommon in many of these cases. All the above-mentioned factors are known to bring about changes in the plasma protein. Moreover, once the condition of amœbic hepatitis or abscess is established, the degree of liver damage will depend on the extent of the lesion and severity of the infection and there may be marked dysfunction of the organ, reflected in the change of plasma protein level and its fractions. It would be interesting to note such changes in these different grades of amœbic infection and to assess their clinical significance. Strangely enough, in spite of the wide prevalence of this disease, little work has been done along these lines.

Methods and materials

In the present work there were 71 cases of chronic amœbic dysentery, 6 cases of acute dysentery and 14 cases of hepatitis including 3 of liver abscess. All the cases were admitted to the hospital attached to the School. Plasma protein was estimated by the copper sulphate drop method of Phillip and van Slyke and fractions by biuret method (Lowe and Chakravarti, 1945).

Results: A. *Chronic amœbic dysentery.*—These patients were admitted to the hospital with symptoms of repeated attacks of loose stools, possibly with a little blood and mucus alternating with periods of constipation, accompanied by slight pain and tenderness in the abdomen, commonly in the area of cæcum, descending and sigmoid colon. The diagnosis of chronic amœbiasis was made in these cases mainly clinically. Laboratory examination of stool was done systematically for 4 or more consecutive days but in only 31 cases cysts of *E. histolytica* were detected and in 3 others trophic forms were found along with cysts. In 6 cases only the trophic form was found. Sigmoidoscopic examination was done in many of them and it helped to clinch the diagnosis in some of the stool-negative cases.

Plasma proteins were determined soon after the admission. Dietetic history revealed that most of them were habituated to the usual diet and in only a few of them there was definite history of restricted diet specially during the

exacerbation of this condition. Plasma proteins and their fraction in these 71 cases are graphically represented in figure 1.

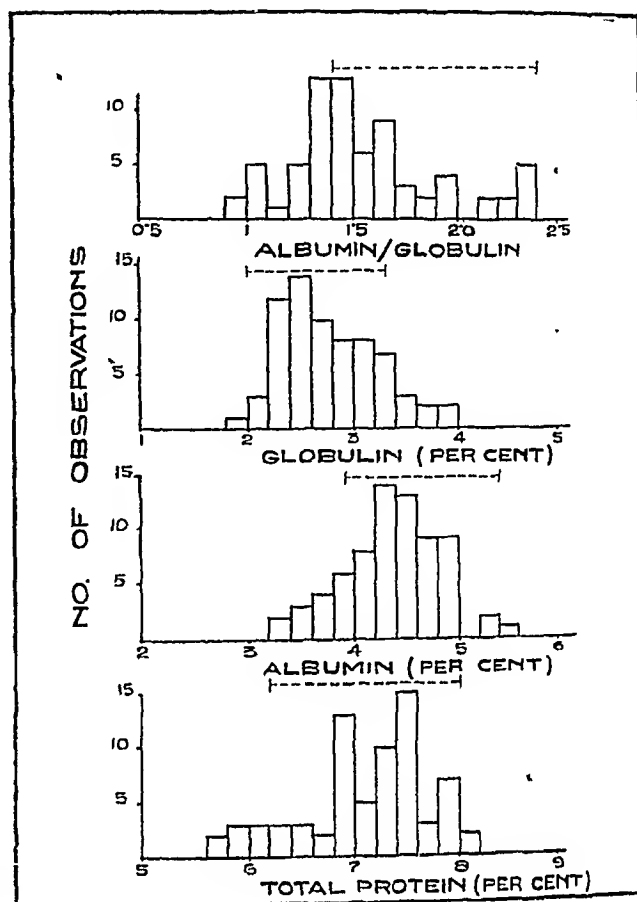


Fig. 1.

Total protein.—In only 8 cases they were definitely lowered (11.3 per cent). Once only it was 8.2 gm. per cent, just above the normal limit. Range—5.6 to 8.2; mean and S.D.— 7.11 ± 0.67 gm. per cent.

Albumin.—In only 12 cases (17 per cent) it was below normal limit. Range—3.2 to 5.6 gm. per cent; mean and S.D.— 4.32 ± 0.49 .

Globulin.—This was within normal range in 64 cases (90 per cent) and definitely higher in 7 cases (10 per cent). Range—1.8 to 4.0; mean and S.D.— 2.8 ± 0.61 gm. per cent.

A/G ratio was normal in all but 25 cases (35 per cent). Range—1.0 to 2.4; mean and S.D.— 1.5 ± 0.38 .

B. *Acute amœbic dysentery.*—Only 6 cases of acute amœbic dysentery were studied. In all of them trophic form of *E. histolytica* was detected in the stool. They came in the hospital with history of acute onset and except one all were admitted within 3 days of the onset of the disease. Results are given in table I and the individual variations are not far from normal. It will be a mistake to overlook the actual hypoproteinaemia which is masked by the associated hæmo-concentration. Albumin and globulin are not equally concentrated as is apparent from the A/G ratio probably due to the fact that some

albumin is lost through the exudation from the gut wall. Case 6 (table I) is a case of chronic malnutrition, admitted in the hospital from a

enlarged tender liver; fever and leucocytosis with increased polymorphonuclear cells. Onset of the disease was very insidious and cannot be dated

TABLE I

Number	Age	Duration of illness and degree of dehydration	Total protein (g m. per cent)	Albumin	Globulin	Albumin/globulin X : 1
1	21	2 days (dehydrated ++)	7.4	1.2	3.2	1.3
2	35	1 day (dehydrated +)	7.2	3.3	3.9	0.8
3	29	3 days (dehydrated +)	7.5	4.8	2.7	1.8
4	18	3 days (dehydrated ++)	8.2	4.5	3.7	1.2
5	40	1 day (dehydrated +)	7.6	3.7	3.8	1.0
6	58	9 days (dehydrated +)	5.8	2.0	3.8	0.55
Total mean (excluding No. 6)			7.6	4.1	3.5	1.17
Normal			7.1	4.5	2.6	1.8

destitute camp and in him the disease was very acute, superimposed over the existing condition of malnutrition. Plasma protein changes are somewhat different in this case, distinct from others.

C. Amoebic hepatitis and liver abscess.—

Eleven cases of amoebic hepatitis and 3 cases of liver abscess are included in this work. Only 7 cases of hepatitis and all the cases of liver abscess gave history of previous attacks of dysentery but in the remaining 4 the diagnosis was made clinically and from the therapeutic response to emetine injection. Cysts of *E. histolytica* were found in the stool of only 3 cases of hepatitis, and in all other cases including the abscesses, stool was negative for four successive days. General picture of hepatitis consisted of complaints of pain in the right hypochondrium,

accurately. Results are tabulated in table II.

Total protein was raised in 2 cases; albumin was reduced in all but 3 cases and globulin was higher in all but 1 case. A/G ratio was normal in only 1 case. Three liver abscess cases deserve special consideration.

Case 1.—A male, aged 50 years, a case of liver abscess, came to the hospital with increasing pain and swelling in the right hypochondrium and upper part of the abdomen. Liver was huge and 6 inches below the costal margin and almost pointing on the outer side of the chest. Hectic temperature, toxic look, profuse sweating, leucocytosis (15,000 cu. mm. of blood with 82 per cent poly), all suggested liver abscess. He gave history of an attack of dysentery 2 years back. Diet was restricted for sometimes due to pain and discomfort.

TABLE II

Number	Name	Enlargement of liver (in inches)	Total protein	Albumin, gm. per cent	Globulin, gm. per cent	Albumin/globulin X : 1
1	K. B.	6 (abscess)	6.8	2.6	4.2	0.62
2	W. B.	2	8.2	4.3	3.9	1.1
3	A. K.	5 (abscess)	7.2	2.0	5.2	0.4
4	G. B.	1	6.5	2.6	3.9	0.66
5	A. L.	3	7.5	2.9	4.7	0.6
6	B. D.	2	7.9	3.51	4.36	0.8
7	J. D.	2	7.5	3.5	4.0	0.9
8	L. M.	2	7.2	3.5	3.7	0.9
9	M. H.	Just palpable and tender.	7.5	4.7	2.8	1.7
10	A. L.	5 (abscess)	9.2	3.3	5.9	0.6
11	B. L.	1½	7.2	1.0	3.2	1.2
12	J. B.	1½	7.2	3.2	4.0	0.8
13	N. S.	2	7.5	3.8	3.7	1.0
14	S. A.	1½	7.5	4.2	3.3	1.3

Total 14 cases—
Arithmetic mean

S.D.

7.5

3.1

4.1

0.9

0.61

0.74

0.80

0.33

Plasma proteins on admission: Total 6.8 gm. per cent, albumin 2.6 gm. per cent and globulin 4.2 gm. per cent.

After repeated aspiration by the author and 9 emetine injections the patient was re-examined after 7 weeks when the liver was just palpable and clinically he was cured. This time total protein was 7.2 gm. per cent, albumin 4.1 gm. per cent and globulin 3.1 gm. per cent.

Case 3.—A male, aged 25 years, admitted to the hospital with history of intermittent fever with rigor and sweating for 2 months along with pain, swelling and a bulging in right hypochondrium. Patient was very much toxæmic and emaciated. Liver was 5 inches below costal margin. He gave history of dysentery 1 year back, treated with emetine. Plasma proteins on admission was—total 7.2 gm. per cent, albumin 2.0 gm. per cent and globulin 5.2 gm. per cent. In spite of repeated aspiration and emetine injection, the abscess opened into the right thoracic cavity and the patient died following a surgical procedure. No follow up of plasma protein was possible in this case.

Case 10.—Another case of liver abscess, already reported by Dr. R. N. Chaudhuri and the present author (1947), came to the hospital with associated secondary infection presumably due to aspiration outside. He had 15 injections of emetine outside; therefore, emetine was not given. He was treated with repeated aspiration, local penicillin instillation and systemic penicillin therapy. The result was remarkable and improvement was accompanied by associated plasma protein changes which tended to become normal. Below are given the findings (table III).

of hypoproteinaemia in these cases while discussing the surgical complications of amœbiasis and opined that hazard in surgery in these cases may be due to hypoproteinaemia which should be well-guarded before any surgical manœuvre is contemplated.

In cases of acute dysentery, in the present series, the plasma protein level was not much lowered probably due to associated hæmo-concentration but the inflammatory exudate and acute infection along with poor food intake would all tend to diminish the plasma protein and the resultant level would be the sum-total of these counter-balancing effects. In view of the present findings it is probable that hypoproteinaemia found by Elsdon-Dew (*loc. cit.*) was a concomitant finding and in one case in the present series, a destitute, similar type of result was observed.

In chronic dysentery unlike many other chronic infections, *e.g.* kala-azar, tuberculosis and leprosy, globulin was found normal in 90 per cent of cases. Probably because chronic amœbiasis is not a generalized infection, no rise in the globulin fraction occurs as it is regarded as a 'host reaction' in a chronic infection. Moreover, even in the presence of occasional diarrhoea, incidence of hypoproteinaemia was remarkably low. Unlike sprue and other chronic diarrhoea, in chronic amœbiasis, nutrient materials including proteins are well absorbed from small intestine and hence hypoproteinaemia due to mal-absorption does not occur in absence of any dietetic restriction.

Hepatic dysfunction in chronic amœbiasis has long been a subject of controversy. Heilig and Visveswar (1944) using hippuric acid synthesis

TABLE III

Date	W.B.C./c.mm. (in 1,000)	Polymorpho- nuclear cells (per cent)	Plasma proteins gm. per cent		
			Total	Albumin	Globulin
18-6-46 (on admission)	16.0	81.0	9.2	3.3	5.9
2-7-46	11.5	76.0	8.9	3.8	5.1
19-7-46	13.0	68.0	7.5	3.45	4.05
6-8-46	10.5	64.0	7.8	3.95	3.95
18-6-46 (on discharge)	5.0	65.0	7.5	3.9	3.6

Discussion

Association of hypoproteinaemia with amœbic dysentery was suggested by Faust (1930), and Elsdon-Dew (1946) examined total serum protein by copper sulphate method in a series of acute amœbic dysentery cases in the natives of South Africa. He found deficiency in serum protein in fulminant amœbic dysentery but whether it was 'ante-hoc' or not was difficult to say in view of the fact that diet was notoriously poor specially in protein in most of them. Recently Therom (1947) opened up the question

test in 15 cases of acute or subacute amœbic dysentery found that 46 per cent of cases had definite impairment of liver function. Gminder (1939) investigating the functional efficiency of liver by Takata-Ara test in 23 patients with amœbic dysentery (9 acute and 14 chronic) found no evidence of liver damage in acute cases but in 71 per cent of chronic cases there was some evidence of parenchymatous liver change. Barbagallo (1936) used the Weltmann coagulation test with a series of patients suffering from amœbic or other colitis and found an increase

of coagulation band in all the cases. Shute (1947) applying C.C.F.T. test found in a series of 73 acute and chronic cases of amoebiasis (excluding those proved to have hepatic involvement) that 50.6 per cent gave evidence of damage to liver parenchyma. So far as the function of fabricating proteins are concerned it appears from the present study that there is little impairment of liver function in these subjects. Depression of albumin fraction and rise in the globulin is the usual picture of the damage to liver parenchyma. In only 17 per cent of the present cases hypoproteinaemia was found and in 10 per cent globulin was high. If in all these cases deficiency in liver function is presumed even then the number of cases having hepatic involvement is very small. It must, however, be emphasized that liver is such a complex organ that its dysfunction cannot be ascertained by any single test.

In amoebic hepatitis and liver abscess plasma protein changes observed are consistent with what is observed in other conditions of liver parenchymatous damage. In general, there is depression of albumin fraction, rise in globulin and A/G ratio tends to be lowered and sometimes even reversed. More remarkable changes are observed in liver abscess than in hepatitis. Total protein is normal, raised or diminished, depending on the rise of globulin fraction. Similar results have been observed both clinically and experimentally in various liver conditions and in hepatectomized animal. Plasma protein changes can be regarded as an important index in amoebic hepatitis and liver abscess. The restoration of functional activity of the liver and of plasma proteins to normal is generally accompanied by clinical improvement after treatment.

Literature gives conflicting reports on the efficacy of liver function test in amoebic hepatitis and abscess. Manson-Bahr (1945), Strong (1945) and others are of opinion that liver function tests are disappointing in such conditions. By using bromsulphthalein retention test, Brown and Hodgson (1938) found a reduction of dye in 8 out of 13 cases of amoebic liver abscess. Hurst (1941) by using laevulose-tolerance test demonstrated hepatic dysfunction in all these cases. Heilig and Visveswar by hippuric acid synthesis test found little evidence of impairment of liver function in 11 cases of amoebic hepatitis, whereas Shute found positive C.C.F.T. test in all his 5 cases of hepatitis. In the present work as judged by plasma protein variation, liver dysfunction was found in almost all the 14 cases of amoebic hepatitis and liver abscess. But the degree of such change in hepatitis is not exactly proportionate to the severity of the case and it is probable that this change can hardly be regarded as an accurate clue to the extent of damage done to the liver parenchyma. But in liver abscess changes are much more pronounced and suggestive of severe

damage to liver cells. In view of the discrepancy observed in various other liver function tests in this condition, estimation of plasma proteins are of immense importance in the diagnosis, prognosis and treatment.

Danger of amoebic hepatitis supervening upon amoebic dysentery during the course of an attack and for many months afterwards must receive attention by the clinician. In chronic amoebiasis, there is hardly any significant change in plasma proteins, whereas as soon as there is hepatic involvement, the picture is changed. Thus routine estimation of plasma proteins in the follow-up of the cases of amoebic dysentery may help an early diagnosis of any hepatic involvement in this condition.

Summary

Plasma protein pattern was studied in 71 cases of chronic amoebic dysentery, 6 cases of acute dysentery and 14 cases of amoebic hepatitis including 3 cases of liver abscess.

1. In chronic dysentery the incidence of hypoproteinaemia was found only in 17 per cent of cases and unlike other chronic infections the globulin was raised only in 10 per cent. Unless diet was restricted plasma proteins were not far from normal, and there was little evidence to show liver dysfunction from plasma protein study in these cases.

2. In acute stage of the disease total protein was not much lowered and due to haemo-concentration absolute hypoproteinaemia was probably masked. Albumin and globulin were not equally concentrated (albumin being lost more) as evident from the A/G ratio.

3. In hepatitis and liver abscess the picture was that of liver parenchymatous damage due to any other causes. Albumin was depressed, globulin was raised. Changes were more marked in the cases with abscess and they tended to return to normal with recovery. The routine estimation of plasma proteins in the follow-up of the cases of amoebic dysentery may help an early diagnosis of any hepatic involvement in this condition.

My grateful thanks are due to Professor R. N. Chaudhuri, under whose guidance this work was done.

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CHLOROMYCETIN IN THE TREATMENT OF CHOLERA

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SINCE the advent of sulphonamides chemotherapy of cholera has been intensely studied, but it has not yielded any uniform results. These drugs have been tried generally with the usual saline treatment but the outcome has been nothing like the dramatic effect as seen in bacillary dysentery. Formo-cibazol was expected to be somewhat more effective but its value appears to be limited. Recently chloromycetin has been shown by Gauld *et al.* (1949) in *in vitro* and *in vivo* experiment tests to inhibit completely the growth of Inaba and Ogawa strains of *V. cholerae*. This observation prompted us to undertake a clinical trial of this drug to determine the actual field of its usefulness in human cases. In this preliminary note are recorded the results of treatment of cholera in ten patients with chloromycetin as compared with ten control cases.

Materials and method.—The patients were Indian males admitted into the Campbell Medical College Hospital during April and May 1950, their ages varying from 8 to 55 years. Clinically they were all typical cases of cholera, and the diagnosis was confirmed in all but two (cases 6 and 11) by the isolation of vibrios from the faeces. All were admitted in the stage of evacuation or of collapse within 5 to 14 hours of the onset of illness and had received no previous treatment. The series included altogether twenty patients; ten were given chloromycetin (chloramphenicol) and alternate ten cases served as control, but they all received the usual saline treatment. Chloromycetin was

given by mouth (administered by one of us) in divided doses, 24 capsules (0.25 gm. each) on the first day and 12 capsules each on the second and third days, altogether 48 capsules in three days. It was started usually after the first saline infusion on admission and when the reaction, if any, was over. Any dose vomited within half an hour was repeated after a short while. Faeces of each patient were examined daily in the Bacteriology Department of the School.

Bacteriological technique

Collection of stool.—In the early stage of the disease the stools were collected, through a sterilized rubber catheter passed into the rectum, directly into a sterilized test tube. No preservative was used, the material being examined within a short time. Later as the stools were formed the patient was made to defaecate on a clean earthen pot and it was then covered with another pot. About two grams of the faeces was transferred to a bottle containing 10 cc. of preserving fluid (Venkatraman and Ramakrishnan, 1941). If the bowels did not move a rectal swab was taken and put in the preserving fluid.

Culture.—Liquid stools were plated directly on the modified Wilson and Reilly's solid medium (Pandit, 1941). In cases of formed stools or rectal swab the material was also enriched by Read's modification of Wilson and Blair's liquid medium (Read, 1939), after 24 hours' incubation, plated on the solid medium mentioned above. Subsequently, several suspicious colonies were picked up and tested by slide agglutination against Inaba and Ogawa specific O sera. Final identification was made by morphological examination, biochemical reaction and tube agglutination. Haemolytic tests were also done with a few strains.

A case was considered bacteriologically negative when at least five consecutive stool cultures showed no vibrio.

Case notes

A summary of the case notes of (A) patient-treated with chloromycetin and of (B) patient not so treated is given in the table.

Results.—Clinically no obvious difference was observed between the two groups of case. Two patients in the treated group died: one (case 7, a boy of 12 years) died 20 hours after admission and the other (case 9, aged 19 year) died 51 hours after admission after they had 3 gm. and 11 gm. of the drug respectively. One of the control group (case 4, aged 38 year) died 72 hours after admission. Bacteriologically rapid disappearance of vibrios from the faeces was the most characteristic feature in those who had the drug; the growth was luxuriant on admission but the number of colonies was markedly reduced in 24 hours and nil by 48

TABLE
Summary of the case notes of the patients
(A) Treated with chloromycetin

Serial number	1	3	5	7	9	11	13	15	17	19
Age in years	55	20	36	12	19	45	36	35	8	30
Duration of illness in hours	8	14	6	5	10	10	14	6	6	9
Dehydration	+++	++	++	++	++	++	++	++	++	++
Pulse on admission	I	I	I	F	I	I	F	I	F	F
Blood pressure (2nd day)	75/40	95/40	90/50	..	90/50	80/45	90/60	100/70	..	90/50
Urine passed within 4 hours of admission.	Nil	Nil	Nil	Scanty	Nil	Scanty	Scanty	Scanty	Nil	Scanty
Vibrios (Ogawa) in stool—										
1st day	+++	+++	+++	+++	+++	—	+++	+++	+++	+++
2nd day	+	—	+	+	+	—	—	—	+	—
3rd to 7th day (onwards)
Total dose of chloromycetin in grammes.	10	11	11	3	11	12	12	12	6	12
Result	C	C	C	D	D	C	C	C	C	C

(B) Not treated with chloromycetin

Serial number	2	4	6	8	10	12	11	16	18	20
Age in years	24	38	30	18	20	25	28	20	26	30
Duration of illness in hours	13	5	8	3	6	12	12	10	8	12
Dehydration	+++	++	++	++	++	++	++	++	++	++
Pulse on admission	I	I	I	F	F	F	F	F	I	I
Blood pressure (2nd day)	100/60	80/40	80/40	90/60	80/45	80/45	90/50	85/45	80/40	90/50
Urine passed within 4 hours of admission	Nil	Nil	Nil	Nil	Scanty	Scanty	Nil	Nil	Scanty	Nil
Vibrios (Ogawa) in stool—										
1st day	+++	+++	—	++	+++	+++	+++	+++	+++	+++
2nd day	+++	++	—	++	+++	+++	+++	+++	+++	+++
3rd day	+++	++	—	—	+++	+++	+++	+++	+++	+++
4th day	+++	..	—	—	+++	+++	+++	+++	+++	+++
5th day	+++	..	—	—	+++	+++	+++	+++	+++	+++
6th day	+++	..	—	—	+++	+++	+++	+++	+++	+++
7th day	+++	..	—	—	+++	+++	+++	+++	+++	+++
8th day	—	..	—	—	—	—	—	—	—	—
Result	C	D	C	C	C	C	C	C	C	C

Note.—I=imperceptible; F=feeble; C=cured; D=died; ++=stool culture positive for cholera vibrios, less than 10 colonies; +++=10-25 colonies; ++++=26-100 colonies; ++++=innumerable colonies; —=culture negative.
All patients (A and B) had Rogers' saline treatment.

hours, while vibrios were isolated from the untreated patients up to the seventh day (see table).

Discussion.—In view of the reported inhibitory effect of chloromycetin on *V. cholerae*, the drug was tried on a series of ten cases of cholera. They were admitted with acute symptoms after an average duration of nine hours in more or less severely dehydrated condition with very low or almost inestimable blood pressure and feeble or imperceptible pulse. The total dosage was about 48 capsules (0.25 gm. each) administered in three days. They received in addition the usual saline treatment like the control group which also consisted of ten cases of similar severity and duration. No difference in the course of the disease or results of the treatment was noticed between the two groups. That there were two deaths against one in the control series is of no statistical importance. Besides, one of them belonged to young age group that stands dehydration badly and had only 3 gm. of chloromycetin. But what was remarkable was the almost complete disappearance of the vibrios within 24 hours of starting the treatment with chloromycetin. This did not make any difference in the ultimate results, but then we must remember that no drug is likely to influence the disease when severe dehydration is present with all its complications (Chaudhuri, 1950). At this stage parenteral fluid is the only procedure that can avert its downward course and this will always be our mainstay in the treatment of cholera. But here we wish to note that chloromycetin by its quick action on the vibrios might be of considerable value as a prophylactic and also against the spread of cholera, though the optimum dose has yet to be determined. For the same reason it is also possible that given in the earliest stage, before dehydration sets in, it may be able to minimize the ill effects and control the course of the disease. It is suggested that trials be made along these lines in a larger series of cases. In our experience neither sulphaguanidine nor formo-cibazol has any marked effect on the excretion of vibrio in cholera patients.

Our thanks are due to Dr. A. K. Dutta Gupta, Superintendent, Campbell Medical College Hospital, for permitting us to carry out this clinical trial and to Messrs. Parke, Davis & Co. for a free supply of chloromycetin.

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A RAPID METHOD OF IRON HÆMATOXYLIN STAIN FOR PROTOZOA IN TISSUE SECTIONS AND SMEARS

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THERE are several well-known methods of iron hæmatoxylin staining of protozoa in smears and tissue sections, viz, Heidenhain's, Mallory's, and Weigert's. In the first two of these methods, the mordant, an iron salt, and the stain hæmatoxylin, are applied separately; and in Weigert's method, the mordant and the stain are mixed up immediately before staining. Though excellent results can be obtained with all the above methods, Heidenhain's method evolved in 1891 is still regarded as the best for permanency and for allowing very satisfactory control over differentiation of the different structures of the cell. But it must be agreed that the method is very time-consuming; up to 48 hours or more may be required for the completion of mordanting and staining, though by the use of the mordant and the stain at a temperature higher than the room temperature, it is possible to shorten the time considerably.

The iron hæmatoxylin stain described in this paper was first introduced by Professor M. N. De at the Pathology Department, Medical College, Calcutta, many years ago. This is an excellent hæmatoxylin stain for general purposes and with slight modification in the process of staining and differentiation, satisfactory results have been obtained in staining certain protozoa in tissue sections and smears.

The hæmatoxylin solution used is ripened with bleaching powder (cf. Anderson, 1923) and exposure to sunlight, and the mordant, an acid iron alum solution, is mixed with the stain immediately before use. About ten minutes are required for staining of ordinary tissues. For general purposes, acid alcohol is used for differentiation and the de-staining is quite rapid. After differentiation, the sections are left in running water till a warm blue-black colour develops. The sections are then counter-stained with eosin, dehydrated, cleared and mounted in the usual manner.

It has been found that if the time allowed for the iron hæmatoxylin stain is prolonged and a saturated aqueous solution of picric acid is used for differentiation, the staining of protozoa in tissue sections and smears is more satisfactory and the different structures in the protozoan cell more easily differentiated. Full details of

this modified method of iron hæmatoxylin staining is given below :

Preparation of the stain

1. *Stock solution of hæmatoxylin*.—Dissolve 10 gm. of hæmatoxylin in 650 cc. of absolute alcohol. Add 350 cc. of distilled water. Then add 25 cc. of a 4 per cent aqueous solution of bleaching powder. Mix. Expose to sunlight for about a month. The fully ripened solution has a deep brown colour. The solution keeps for months.

2. *Acid iron alum solution*.—Dissolve iron alum 2 gm. in 98 cc. of distilled water and add 2 cc. of concentrated sulphuric acid. The solution is almost colourless or has a very light yellowish tinge.

To one volume of the acid iron alum solution add two volumes of hæmatoxylin solution. Mix. This iron hæmatoxylin stain is prepared immediately before use.

Method of staining protozoa in tissue sections

1. Fix in Zenker or suitable fixative.
2. Embed in paraffin and cut sections 4 to 5 microns thick.
3. Remove wax with xylol, xylol with alcohol and then transfer successively to rectified spirit 90 per cent and 70 per cent alcohol and water.
4. Remove mercury with Lugol's iodine, iodine with 0.5 per cent 'hypo' solution in water and wash in running tap water for 5 minutes.
5. Stain with iron hæmatoxylin stain prepared as described above for 15 to 20 minutes.
6. Wash in tap water till the section appears black in colour.
7. Differentiate with a saturated aqueous solution of picric acid. For tissue sections about 1 to 5 minutes or a little longer is required for a satisfactory degree of differentiation. The section is de-stained with picric acid for 1 to 2 minutes, washed in water, and then examined under the microscope using high power to see if the differentiation is satisfactory or not. If the protozoa are still overstained, it is again covered with picric acid and the whole process repeated till the differentiation is satisfactory. The section is then left in running tap water for about 5 minutes to wash out most of the picric acid stain. (70 per cent alcohol and rectified spirit may be used for removing the picric acid stain, but the section has to be brought down to water before the next stage.)
8. Counter-stain lightly with a weak watery solution of yellowish eosin, controlling the depth of staining with the microscope. Wash in water.
9. Dehydrate, clear and mount in balsam.

Note.—With a little experience it is possible to differentiate with acid alcohol (1 per cent sulphuric acid in rectified spirit), but the de-staining is rapid and somewhat difficult to control. Acid alcohol is dropped on to the section with the slide held in a slightly slanting position so that the acid alcohol rinses the section and runs down the slide. This is done once or twice and the section is washed in running tap water for a short time and examined under the microscope to see if the differentiation is complete. The process is repeated if necessary and the section is then left in running tap water for 10 minutes to 'blue' it.

Counter-staining with eosin is not essential. The slight yellow colour of picric acid that is left after washing the section serves as a counter-stain and the nuclear details show very distinctly.

With this method of iron hæmatoxylin stain, the cell nuclei appear dark blue-black to black, the nucleoli and the chromatin net-work or granules are well shown.

Method of staining protozoa in smears

1. Fix in Schaudinn's fixative for 20 minutes.
2. Rinse in 50 per cent alcohol and then transfer to 70 per cent alcohol to which enough alcoholic iodine has been added to give it a port wine colour. Soak for 20 minutes.
3. Transfer to 70 per cent alcohol, and then to rectified spirit; leave for an hour or longer.
4. Rinse successively in 90 per cent and 70 per cent alcohol and bring down to water.
5. Stain with iron hæmatoxylin solution for 20 to 30 minutes. Wash and soak in tap water till the smear appears dark black.
6. Differentiate with saturated aqueous solution of picric acid for 1 to 6 minutes, controlling the de-staining with the high-power microscope using 10 X eye-piece. When the differentiation is satisfactory, leave in gently running tap water for 5 to 10 minutes to wash out most of the picric acid stain.
7. Counter-staining is not generally necessary.
8. Dehydrate, clear and mount in balsam.

Note.—Plasmodia and hæmoflagellates are more readily stained with the Romanowsky stains. Even in tissue sections excellent results comparable with those obtained in smears may be obtained with Giemsa stain as described by Shortt and Cooper (1948).

For smears of leishmanial flagellates, fixation with osmic acid vapour and Schaudinn's fluid followed by the method of staining as described above gives good results. But the time required for differentiation is shorter, $\frac{1}{2}$ to 2 minutes.

This method of iron hæmatoxylin staining, as modified from that introduced by Professor M. N. De, is rapid and allows a relatively easier

control over differentiation of the nuclear structures of protozoa and the stain is more or less permanent, lasting for several years at least. The photomicrographs (figures 1, 2 and 3, plate XLVI) show the results obtained in staining some protozoa in tissue sections and smears.

Summary

A rapid method of iron hæmatoxylin stain is described for staining protozoa in tissue sections and smears. The hæmatoxylin solution is matured by the addition of bleaching powder and exposure to sunlight. The mordant, an acid iron alum solution, is mixed with the stain immediately before use. For differentiation, saturated aqueous solution of picric acid is used.

We are thankful to Dr. M. J. Miller and to Dr. G. N. Sen for some of the specimens used for staining.

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EXPLANATION OF PLATES XLIV TO XLVI

- Fig. 1.—Note the short left ulna with its styloid process made further prominent by an exostosis and the bent fingers (right middle and ring and left index fingers).
- Fig. 2.—Note the protuberances at the upper end of left arm and near both knees.
- Fig. 3.—Note the multiple exostosis at the upper ends of both humeri. The pedunculated one on the left side pointing towards the middle of the shaft.
- Fig. 4.—Note the short right ulna and the exostosis at its lower end giving an appearance of cavitation in the bone because of overlapping of the cancellous exostosis in the metaphysis. Note also the exostosis at the bases of some of the phalanges.
- Fig. 5.—Note small exostoses along the crest of the ileum on the side (better visible in the original skiagram) and lack of tubulation in the necks of the femora.
- Fig. 6.—Note the large pedunculated exostosis arising from the posterior surface of femur and another one giving an appearance of cavitation of lower metaphysis. On the right side note the exostoses from the lower end of femur and the large cauliflower-type exostosis at the upper end of fibula from which a biopsy was taken.
- Fig. 7.—Photomicrograph of biopsy specimen (low power $\times 130$). Note the hyaline cartilage, the transitional zone and the cancellous bone with one of its septa enclosing fatty bone marrow cells.
- Fig. 8.—Same as 7. Magnification $\times 430$ (high power).

A Mirror of Hospital Practice

A CASE OF HYDRONEPHROTIC KIDNEY

By K. G. SOLANKI, L.M.P. (Bom)

Assistant Medical Officer, Bhavsinhji Hospital,
Poibandur

A HINDU female child, aged 9, was admitted to the hospital for enlargement of the abdomen.

Duration.—Since childhood.

Past history.—Three months after birth, a swelling of the size of an orange was noticed in the left lumbar region. A needle was put in with no result. Subsequent treatment with electrotherapy produced no change in its size.

Progress.—The swelling went on increasing gradually without giving rise to any symptoms pertaining to any system except heaviness in the abdomen.

Examination: (1) *Local inspection.*—Generalized enlargement of abdomen, more on the left flank (figures 1 and 2, plate XLVII).

(2) *Palpation.*—Elastic feel of the abdomen with no definite outline of the enlargement made out. Tenderness. Fluid thrill +.

(3) *Percussion.*—No shifting dullness. Dullness +.

(4) *Auscultation.*—No sounds heard.

(5) *P. V. examination.*—Not made.

(6) *Urine and blood examinations.*—Nothing particular.

Operation

Right paramedian incision was made extending from just below the costal margin to a point four inches below the umbilicus. After incising posterior rectus sheath, large tense swelling was visible. Peritoneum was difficult to find because it was pushed to the right so much by the tumour that incision directly opened up the extraperitoneal space and the incision exposed the lateral side of the descending colon.

On exploring the tumour, 5 cc. fluid, watery and odourless, was aspirated. On separating the tumour from the surrounding structures, mesenteric cyst was suspected but no connection with mesentery was found. The tumour was getting the blood supply from aorta at the site of renal arteries. Then the tumour burst all of a sudden and about 3 pints of fluid came out. On examination, both ovaries, liver, spleen and right kidney were normal but left kidney was not found at all. On further dissection downwards, tumour was found connected with a cord-like structure following the course of ureter



Fig. 1.

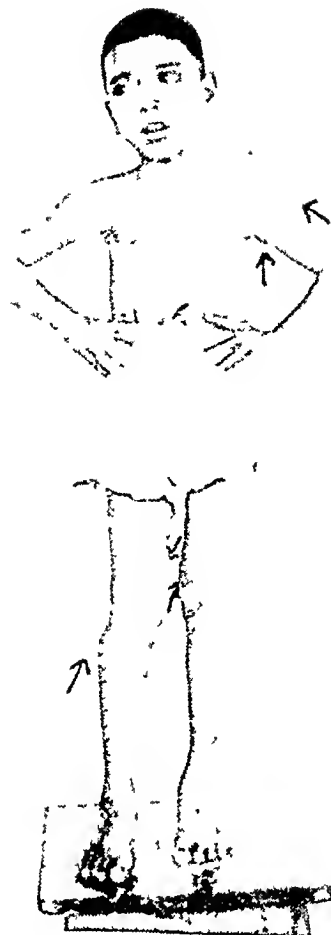


Fig. 2.



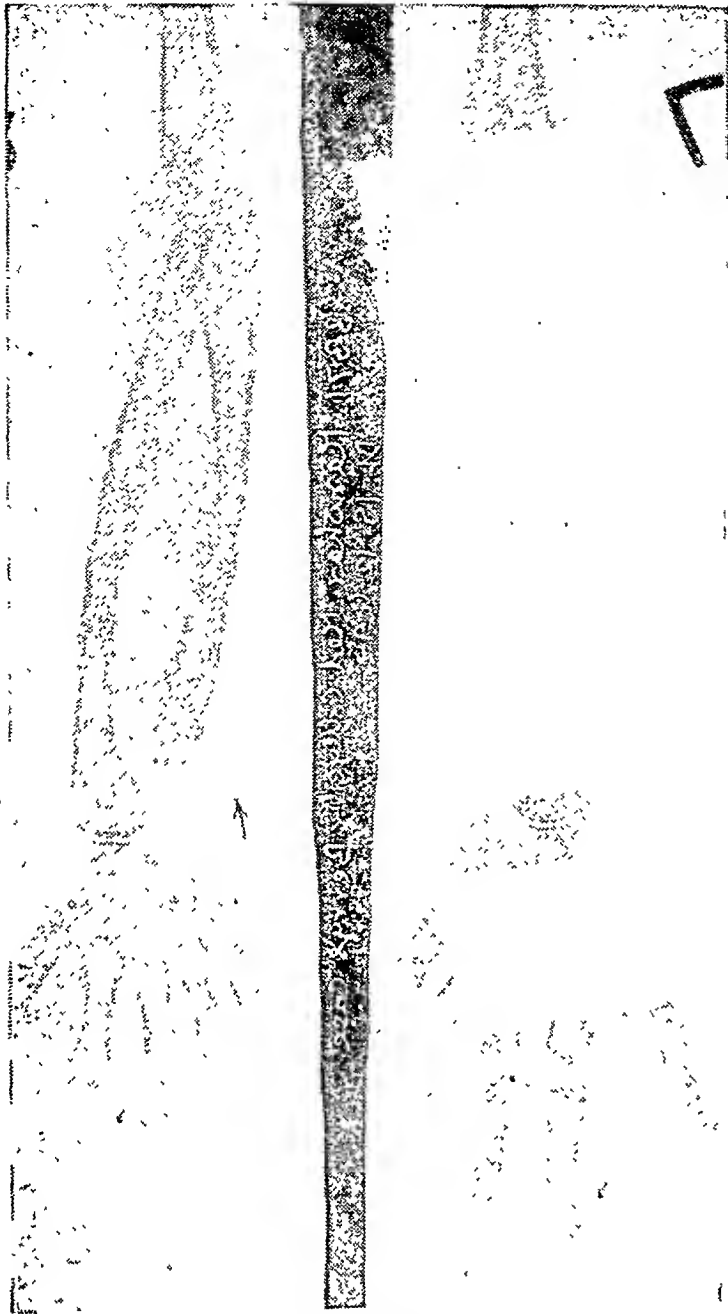


Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.

METAPHYSIAL ACLASIS : J. N. BERRY. (O. A.) PAGE 387
(For description see page 402)

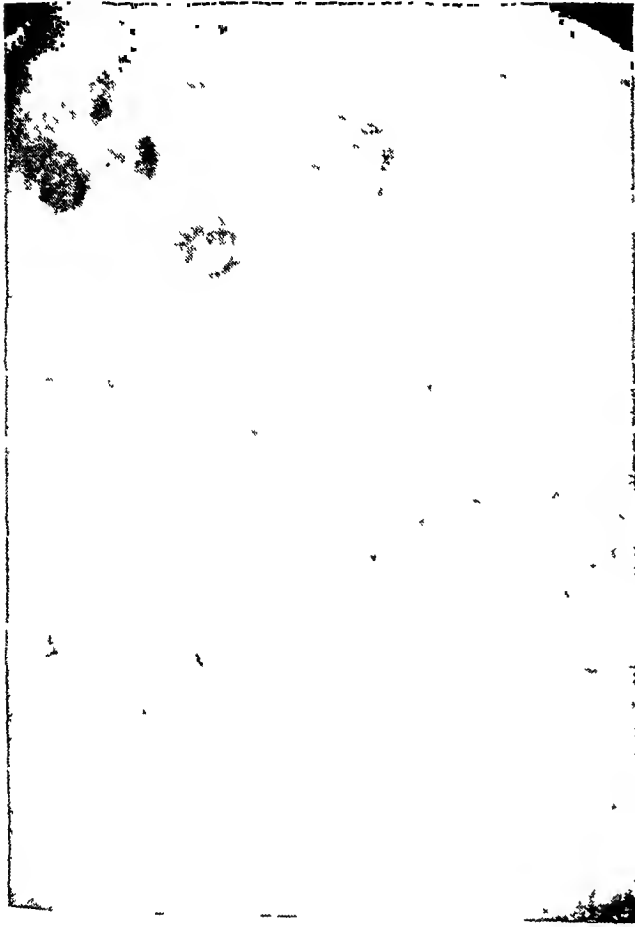


Fig. 8

A RAPID METHOD OF IRON HÆMATOXYLIN STAIN
FOR PROTOZOA IN TISSUE SECTIONS AND SMEARS :
P. C. SEN GUPTA, K. C. BASU MALICK AND
B. BHATTACHARYA. (O. A.) PAGE 100

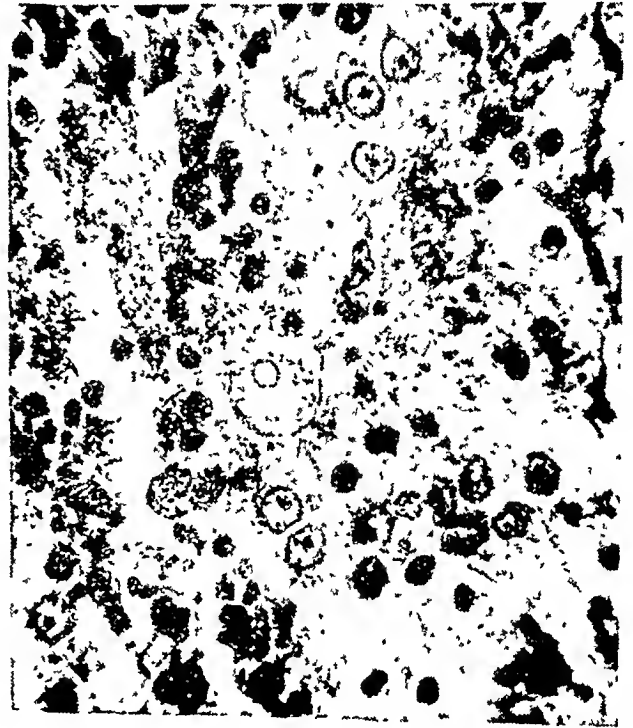


Fig 1.—*E. histolytica* in liver abscess of a cat

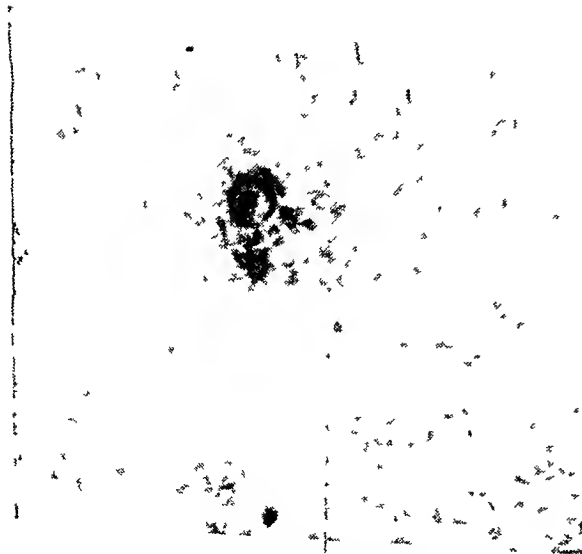


Fig. 2—*E. histolytica* in faecal smear.



Fig 3—*Leishmania donovani* in a section of liver from a case of kala-azar

which was later found out to be ureter connected with bladder and the tumour was large hydronephrotic kidney. Nephrectomy was performed and abdomen was closed up as usual. On opening up the removed specimen (figure 3, plate XLVII), it was found out to be a complete bag of water. Patient passed urine next morning and has done so without any trouble since. She made an uneventful recovery and was discharged cured on the fifteenth day. A month after the discharge she was photographed (figures 4 and 5, plate XLVIII).

My grateful thanks are due to Dr. H. H. Chavda, Additional Chief Medical Officer, Sorath, Porbandar, for permitting me to send this case report for publication.

P.S. The incision was made on the right side because prior to exploratory laparotomy no definite diagnosis was arrived at and as the tumour was protruding more on the right side.

A CASE OF CEREBRAL MALARIA

By K. D. JAIN, M.B., B.S.

U. P. Military Police Hospital, Sitapur

P. S., a Hindu male, 20 years, was admitted on 2nd August, 1949, at 7 a.m. in an unconscious state with gasping type of respiration.

History of present illness.—The patient was feeling out of sort and getting 3 to 4 stools a day. He had no appetite also for the last three days.

On the morning of 2nd August, 1949 at about 6.30 a.m., he was getting his hair cut. After finishing it, he got up and walked about 2 to 3 steps and fell down in a semi-unconscious condition. Thereafter, the patient was taken by the friends to hospital.

Examination.—The patient was unconscious and corneal reflex was absent. Pupils moderately dilated not reacting to light. Pulse 70 per minute. Tension and volume weak. Respiration 10 per minute, irregular, shallow and failing. Rectal temperature 96°F.

Heart sounds muffled and distant.

Spleen and liver not palpable. Other organs normal.

After this hurried examination it was noticed that the respiration had stopped.

Artificial respiration was given for about five minutes before the patient could be given coramine subcutaneously. Then respiration re-started and 100 cc. of 25 per cent glucose solution were given I.V. and 1 cc. adrenalin solution was given subcutaneously.

After that the patient went into a condition of stupor with vacant looks. His head was moving from side to side; eye-balls rolling up and down. He was weeping at intervals and asking for his friends, though he could not recognize anybody.

When this particular type of stupor, which I term 'as restless searching type of stupor' was noticed, I thought of the provisional diagnosis of *cerebral malaria*, a few cases of which in this particular stupor were seen previously. Thereon four tablets of paludrine after powdering them were given to the patient to swallow with an ounce of stimulant mixture.

Blood film was examined. 'M.T. rings' were detected and the diagnosis was confirmed.

Quinine (6 grains to 1 cc.) was injected intramuscularly and the patient was put on further three tablets four-hourly. At about 10 a.m., patient showed signs of regaining consciousness. Another 100 cc. of glucose 25 per cent solution were given I.V. The patient maintained 99.2°F. temperature. In the evening at about 4 p.m., the patient complained of severe type of colicky pain in the abdomen with great nausea. Nothing could account for this and the patient was fully conscious.

Thinking it to be due to an overdose of paludrine the drug was discontinued till next morning, when he was given one tablet t.d.s. Next morning, the temperature was 101.2°F. and finally the patient settled down on 5th August, 1949, and he was discharged cured on the 10th, with the advice to continue prophylactic treatment one tablet twice weekly for three months.

Summary of the case.—(1) A typical type of cerebral malaria with no rise in temperature.

(2) Peculiar type of stupor which is termed as 'restless searching type of stupor', the key point in the diagnosis.

Cases of cerebral malaria are not uncommon in the tropical countries, where the diagnosis is not difficult provided one keeps in mind this entity and this type of picture.

The type should be given priority even over blood film examination in a country like ours where facilities for microscopic work are very meagre, even in urban areas and nil in rural areas.

The peculiar stupor mentioned above was also seen by me in few other cases of cerebral malaria with hyperpyrexia.

My thanks are due to Dr. S. N. Chatterjee, Civil Surgeon, Sitapur, for kind permission and advice to report this case.

UTERINE MANIFESTATIONS OF VITAMIN-B DEFICIENCY

By M. S. WAGLE, L.M.S.

Gadag

A good deal of literature is being published for many years past, on vitamin deficiency, and its effects on the human body. Vitamin B deficiency is the commonest of all. Signs and symptoms like loss of appetite, raw tongue, ulcers at the corners of mouth, diarrhoea, redness of conjunctiva, burning sensation in hands and feet and even in urethra, itching and neuritis are known to all the practitioners. But so far I have not read anywhere about pains in a gravid uterus, simulating threatened abortion, being caused by vitamin B deficiency. And hence the following case notes will interest your readers :—

Mrs. H., an apparently healthy young lady of about 25, came to my dispensary on 30th June, 1949, with a lutocyclin ampoule and asked me to give that injection to her. I could not examine her, as I was not asked to do so, but a casual talk brought out the following history. She was 3rd para, pregnancy about 6 months, and was having pains, simulating uterine contractions, for some time past. No history of any previous abortion. Both the issues are

healthy. She had consulted an obstetrician elsewhere. He gave her a lutocyclin injection, prescribed uterine sedatives, and advised her to take 6 more injections.

She followed the advice correctly. She took the subsequent injections on 2nd June, 5th June, 11th June, 17th June and 23rd June, 1949. In spite of this treatment there was no relief. On the contrary the pains increased. She developed insomnia. Gardinal $1\frac{1}{2}$ gr. did not give her good sleep. She consulted the obstetrician again. He changed the medicines. But even these did not give her any relief.

She came to me again on 1st July, 1949, complaining of anorexia, raw tongue, and diarrhoea. She wanted me to treat her. On examining I found her to be a typical case of B deficiency. I gave her an injection of B-complex and B-complex tablets. Her report next day gave me a pleasant surprise. Her other complaints had not improved, but there was a definite relief in her uterine pains, which had persisted till that day, and 2 more injections on alternate days gave her complete relief. I had to give her further 3 injections for the relief of other complaints, and after that I stopped all treatment.

After complete relief for 26 days the uterine pains reappeared on 31st July, 1949. By this time the pregnancy had advanced to 8 months. To make sure that this time at least these were not false pains, I treated her with uterine sedatives for 3 days. Finding no relief, I started B-complex treatment. Three injections gave her complete relief. On 3rd September, 1949, she gave birth to a healthy child. I was told that both her previous confinements were breech presentations, and required medical interference. This time it was vertex presentation, and a normal delivery.

Discussion

Pains in a gravid uterus simulating threatened abortion, which had defied intensive treatment with uterine sedatives, for more than a month and a half, disappeared with 3 vitamin B-complex injections. They reappeared after 26 days. Sedative treatment for 3 days had no effect. Three more injections of vitamin B-complex gave her complete relief.

Indian Medical Gazette

SEPTEMBER

ATOM BOMB MADE EASY

ONE isotope of uranium U235 (uranium with atomic weight of 235) when struck by a neutron is capable of being split into radioactive fragments of less atomic weight, with release of energy. As the splitting proceeds new neutrons are produced. If they are passed through graphite and controlled in the atomic pile they are capable of splitting more U235. An atom bomb is an atomic pile in which the control is absent. Thus is set up a chain reaction resulting in a violent explosion. One pound of U235, when only 5 per cent of the isotope is split, causes more destruction than 100 tons of T.N.T. (Routh, 1949).

To digress into physics of the early medical studies: (1) Atoms are made of positive electric units called *protons*, negative electric units called *electrons* and neutral electric units called *neutrons*, made up of one proton plus one electron—not always present. (2) Every atom consists of a *nucleus* of protons (and sometimes of neutrons as well) surrounded by electrons which revolve round it as the planets revolve round the sun. The revolving electrons (as opposed to the electrons fixed in the neutrons) are the *planetary* electrons. (3) The mass, weight for all practical purposes, of an atom is the weight of the protons in the nucleus (free or in neutrons). The electron has a negligible mass, $1/1845$ of a proton. The atomic weight of an element is the weight of its nucleus. (4) The planetary electrons correspond in number to the free protons in the nucleus. Their number in an atom of an element is the *atomic number of the element*. The *atomic weight* may be more than the atomic number because of the protons combined with electrons in the neutrons. (5) The planetary electrons occupy space and are thus limited in orbits: only 2 can exist in the 1st orbit which is closest to the nucleus, 8 in the 2nd orbit and 18 in the 3rd. (6) The lightest atom is that of the light hydrogen which is composed of 1 proton and 1 electron. Its atomic number is 1 and atomic weight is 1.0078. (7) The heavy hydrogen is composed of 1 proton, 1 neutron and 1 electron. Its atomic number is 1, but atomic weight is 2.0143. The mixture in naturally occurring hydrogen has an atomic weight of 1.008. The heavy water is composed of heavy hydrogen. After its discovery many years ago many attempts were made to find a use for it in medicine but it has remained useless. The heavy hydrogen provides the most destructive weapon man can make, the hydrogen bomb, which is a direct descendant of the atom bomb. (8) The

light hydrogen and the heavy hydrogen are isotopes. The difference is due to the neutron. All elements have isotopes.

U235 is an isotope of the ordinary neutral uranium, U238. It provided the first atom bomb used in Japan at Hiroshima. The devastating power of the bomb equalled that of 20,000 tons of T.N.T.

From the neutral form of uranium, U238, were produced in the atomic pile (constructed with graphite) new elements neptunium (atomic no. 93) and plutonium (atomic no. 94). Plutonium also lends itself to splitting. The second atom used in Japan at Nagasaki was a plutonium bomb.

Here is a description by the survivors of what occurred at Hiroshima. A blinding instantaneous flash of white or green light was seen and with it came intense heat and immediately after was felt the shock of detonation. The flash was the electro-magnetic radiation in the visible range and the heat came from ultra-violet, infra-red and visible rays. The heat, unlike the blast of hot gas which goes round bodies, only burnt the exposed side. Its intensity was great, 1,200 to 2,000°C. within 500 yards of the ground centre of explosion, but its penetration was poor; skin was completely protected by thin clothing. The intensity of penetration of the neutron and gamma rays, on the other hand, was terrific. In the concrete Red Cross Hospital at Hiroshima, 2,000 yards from the ground centre of explosion, x-ray films stored in a lead vault were ruined. Thousands of people who thought they had escaped because their skin was not burnt had received exposure which proved fatal after weeks or months. It had destroyed their hæmopoietic system. It had also injured their gonads (Anderson, 1948).

Radiation sickness started within an hour or so with fever, nausea, vomiting and diarrhoea. Lymphopenia and leucocytopenia developed soon. Anæmia developed later. Fatal cases were characterized by a terminal rise in temperature, ecchymosis and hæmorrhage. Bleeding appeared to be due to the presence of heparin, not thrombocytopenia. Secondary infection was due to agranulocytosis. Many who were not badly exposed developed lassitude, anorexia and cachexia of radiation after several days or weeks. Damage to the gonads was not permanent; obviously, all survivors had received only sub-sterilization doses (Anderson, *loc. cit.*).

Here is an abstract from the recently published British textbook on Civil Defence against atom raids. One bomb like those dropped in Japan, bursting in the air over a British city, would ruin in a one-mile radius from the centre of the explosion 30,000 houses; in a further $1\frac{1}{2}$ -mile radius 35,000 houses will need major repairs and no less than 100,000 houses minor repairs. It will affect the homes of 400,000 people. Civil defence workers of the atom raids will visit the ruins in a respirator, denim overalls, rubber gloves and gum boots.

They will carry a disimeter of about the size of a fountain pen to measure the radiation on them. A bigger meter will be carried about to measure radiations in areas. Hospitals will have a more sensitive 'contamination meter'. Back garden shelters of the last war would be useful. Brick and cement stop radiation better than wood (*Daily Press*, 1950).

The contamination is caused by fission products attaching themselves to dust. They are soon dispersed on land. Secondly, induced radio-activity within human bodies or other objects at Hiroshima was found to be of no importance. The fission products trapped by water at Bikini, in the experimental explosion under water, lasted, on the other hand, many months (Anderson, *loc. cit.*).

American radio has supplied further informations: As soon as the bomb is exploded there will be a sudden increase in the intensity of light. A similar effect, however, may be produced by a meteorite hitting the earth. About three and a half years ago such an event was witnessed by the inhabitants of a Siberian Village of Novopokrovka, a few hundred miles from Vladivostock (Unesco Feature no. 27, 15th August, 1950; reproduced in this issue on page 422).

Such will be the effects of the bombs of yesterday. The bomb of to-day is more destructive. It is the hydrogen bomb in which heavy hydrogen is hit by neutrons at a temperature of 100 million degrees. This temperature is produced by the burst of the ordinary bomb of yesterday. The destructive power of hydrogen is 8 to 10 times that of uranium or plutonium (Saha, Lyon's Medical Jurisprudence for India, in press).

The mother of these weapons of destruction is the atomic pile of nuclear physics laboratory.

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Medical News

NOTIFICATION

(No. F.10-23/49-D.S., Government of India, Ministry of Health, New Delhi, 31st August, 1950)

THE following draft of a further amendment to the Drugs Rules, 1945, which it is proposed to make in exercise of the powers conferred by Sections 12

and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections for the information of all persons likely to be affected thereby, and notice is hereby given that the said draft will be taken into consideration on or after the 10th December, 1950.

2. Any objections or suggestions which may be received from any person with respect to the said draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENT

In sub-rule (1) of Rule 97 after clause (b) the following clause shall be inserted, namely:—

'(c) If it contains a substance specified in Schedule H, it should be labelled with the words:—

'Warning.—To be sold by retail only on the prescription of a Registered Medical Practitioner!'

(Sd.) J. N. SAKSENA.

Under Secretary.

QUARANTINE RESTRICTIONS

PRESS NOTE

(Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta, Directorate-General of Health Services, New Delhi, 30th August, 1950)

INFORMATION has been received by the Director-General of Health Services from the health authorities in Ceylon that quarantine restrictions have been imposed against arrivals from Bombay on account of cholera.

In order to avoid delay and inconvenience on entry into Ceylon, passengers leaving Bombay are required to produce international certificates of inoculation showing that inoculation has been performed not less than seven days and not more than six months prior to arrival in Ceylon. The certificate should show that the inoculation was given in two doses with an interval of seven to ten days.

THE SECOND ANNUAL ALL-INDIA CONFERENCE OF INDUSTRIAL MEDICINE (17TH, 18TH AND 19TH DECEMBER, 1950, AT JAMSHEDPUR)

UNDER the auspices of the Society for the Study of Industrial Medicine, India, the Second All-India Annual Conference of Industrial Medicine will be held on 17th, 18th and 19th December, 1950, at Jamshedpur. The Hon'ble Minister Rajkumari Amrit Kaur, Minister of Health, Dominion of India and President of the 'World Health Organization' for the present session has very kindly consented to inaugurate this Conference.

Those who attended the First All-India Conference of Industrial Medicine held during December 1949 need no introduction to it. They may also remember that at that Conference Jamshedpur was selected again as the venue of the second conference.

The object of the Conference is to bring together all the medical officers associated with industry, and to exchange ideas and to work in co-ordination, thus giving an incentive to their work and furthering the cause of industrial medicine. At present when India is being rapidly industrialized and the industrial medicine is in its infancy, the need for co-ordinated scientific planning of industrial medicine cannot be over-emphasized.

At this Conference, as the name indicates, are invited all the medical officers associated with the industry. It is, therefore, the duty of all the medical officers associated with the industry to attend this Conference as is the duty of all the industrialists to send delegates to this Conference.

The First Annual Conference was undoubtedly a great success and the success of the second conference depends on the industrial medical officers wholeheartedly participating in it as well as the industrialists supporting it. All medical officers associated with the industry are, therefore, invited to attend this Conference and, if possible, to read papers on different aspects of industrial medicine.

The Council of the Society for the Study of Industrial Medicine will make arrangements for accommodation, etc. Those who wish to attend the Conference and those who wish to read papers are requested to communicate to the Honorary Secretary, Society for the Study of Industrial Medicine, c/o Tata Main Hospital, Jamshedpur, as soon as possible as the agenda is to be made before November and accommodation is very limited.

The programme will include inauguration ceremony by the Hon'ble Minister Rajkumari Anrit Kaur, exhibition of safety devices in industry, scientific sessions at which scientific papers will be read, dinner of all the delegates and their families, visit to Tisco and associated companies, visit to Tata Main Hospital and a tour of the sites of Jamshedpur, and also film shows where films of interest to the industrial medical officers will be displayed.

THE TUBERCULOSIS PROBLEM IN INDIA

(Supplied by the Tuberculosis Association of India)

THE problem of tuberculosis is to-day recognized as one for the solution of which international co-operation is essential. The World Health Organization Expert Committee on Tuberculosis has summed up the position thus: 'There can be no isolation in the field of health. The fight against infectious diseases is not a national or racial problem. It is a task for the whole of humanity. The all-inclusive objective of any sound tuberculosis programme is the prevention and eventual eradication of tuberculosis from the peoples of the world'. The first Assembly of the World Health Organization recognized tuberculosis as a problem requiring top priority among the programmes carried out under the auspices of that organization.

2. India is playing her part in evolving a tuberculosis control programme, which is in line with those accepted by international health organizations. On a consecutive estimate, there are about 500,000 deaths every year in India due to tuberculosis and there are about 2,500,000 cases of active tuberculosis in this country. Next to malaria, tuberculosis is responsible for the largest number of deaths in this country. Death from tuberculosis is estimated to be very high in the larger cities varying from about 200 to 500 per 100,000 of population. Little information, however, is available from rural areas, but certain investigations have shown that in small towns the infection rate is almost as high as in the larger cities, and that in the villages it is lower but still considerable, and tending to increase. Its ravages are particularly devastating, since it attacks and kills without discrimination, and the tragedy very often is that it is mostly the young who ought to be the wealth and the mainstay of the nation that becomes its prey.

3. Conditions favourable for the spread of the infection and the high mortality are all too common. Standard of living in the country is low, and housing conditions are poor and inadequate. There is much

overcrowding especially in the cities and towns which, during the last ten years, have doubled or trebled their population without corresponding increase in the number of houses. These conditions have become still worse after the partition of India because of the migration of large groups of population from one part of the country to another. There is malnutrition and this has been accentuated in recent years by food shortage and the high cost of living. Hygienic conditions are far from satisfactory and there is a vast amount of ignorance regarding hygienic laws.

4. The improvement of the general standard of living, provision for isolation and treatment of patients, and introduction of preventive measures are the three important measures needed for controlling tuberculosis. As tuberculosis is an infectious disease, the best way to deal with the problem is to isolate all open cases. This has not, however, been achieved in any country in the world, and in India, under the existing conditions, it is impossible to attempt satisfactory isolation of even a small proportion of our infective cases. Improvement of the standard of living, including improvement in housing, sanitation and nutrition, is admittedly one of the important factors connected with tuberculosis control, but the country should also provide for an adequate tuberculosis service, including provision for the after-care and rehabilitation of patients discharged from the hospital. According to standards accepted by tuberculosis workers in all countries, India would need 3,000 to 4,000 tuberculosis clinics or dispensaries and about 500,000 beds for tuberculous patients. Against this we have only 119 clinics and 12,000 beds distributed in 45 sanatoria and 32 tuberculosis hospitals in the whole of India. Calculating on an average of one lakh of rupees for a clinic, including x-ray and other equipments, the total cost of these is likely to be about Rs. 40 crores. The building and equipping of hospitals' sanatoria to provide 500,000 beds at the rate of Rs. 8,000 per bed would cost Rs. 400 crores. If these two items are planned for over a period of 15 years, we need a yearly expenditure of about Rs. 30 crores. To this have to be added the annual expenditure for the running of these institutions, which will be Rs. 60 crores when all the institutions are working. The personnel needed for manning these institutions are roughly 15,000 doctors, 50,000 nurses and 12,000 health visitors as against about 300 doctors and 400 nurses and health visitors available at present. What is spent on medical relief and public health in the whole of India to-day is roughly half a rupee per head of the population, and what is spent on tuberculosis is about less than 1/24 of a rupee. From this it is obvious that India cannot find the necessary means to provide for the minimum requirements in respect of tuberculosis for many years to come. Therefore, in the earlier stage of the tuberculosis campaign, only what is likely to be practicable should be attempted.

TUBERCULOSIS INSTITUTIONS

(a) *Tuberculosis clinics*.—Though the demand for hospital accommodation for tuberculous patients living in crowded homes is pressing, priority should be given to the establishment of tuberculosis clinics. These clinics, in the first instance, should be in cities and towns and from these centres rural areas can be reached by the provision of mobile units. Besides its main diagnostic and advisory work, a clinic in India has to undertake artificial pneumothorax treatment as well as supervise domiciliary treatment.

(b) *Hospitals and sanatoria*.—During the last 7 years only about 2,500 beds for tuberculous patients have been added in the whole of India, that is about 330 beds per year. A definite and concerted effort has to be made to increase the number of tuberculosis beds in the country by at least 2,000 beds per year during the next five years. Even then, we will have only 20,000 beds, as against the 500,000 we need. As a hill sanatorium or hospital away from cities can serve only

a small proportion of tuberculous patients living in congested areas, institutions should, as far as possible, be established in or near crowded areas.

TRAINING AND DEMONSTRATION CENTRES

There should be a few model tuberculosis centres which should serve as teaching and demonstration units. Each centre should consist of a clinic, a hospital or a sanatorium, and, if possible, an after-care colony. These centres should demonstrate practical methods of tuberculosis control, with special emphasis on the preventive aspect rather than on the curative. Medical students, nurses, health visitors, laboratory and x-ray technicians as well as post-graduate doctors are to be trained here. Three such centres are being developed in India at present with the help of the United Nations International Children's Emergency Fund and the World Health Organization, one each in Delhi, Patna and Trivandrum. The establishment of seven more such centres is under consideration.

AFTER-CARE COLONIES

There is an increasing recognition of the need for rehabilitation centres or work colonies for ex-tuberculous patients. A large proportion of tuberculous patients are subject to relapses and, unless suitable work is found for them with provision for sheltered life under medical supervision, much of the efforts spent on putting them on their feet will be wasted. Even so, it is doubtful, whether we are in a position to develop such rehabilitation centres on an extensive scale at present. The demand for isolating and treating infective cases will need most of the resources available. There is only one ex-patients' colony in India at present and this is attached to the Union Mission Tuberculosis Sanatorium, Madanapalle. One is being built in Madras to be associated with Tambaram. Also the Tuberculosis Association of India had recommended to the Central and State Governments, Railway administration and employment bureaux of private agencies, such as business firms, local bodies, industrial organizations, etc., to employ persons who have had tuberculosis but have been certified, after treatment, by recognized tuberculosis specialists, as non-infective and fit for work.

THE RÔLE OF NON-OFFICIAL ORGANIZATIONS IN THE CAMPAIGN AGAINST TUBERCULOSIS

One of the first things to be done in any effective anti-tuberculosis campaign is to create in the minds of the public and the administrators a proper appreciation of the seriousness of the problem and the urgency of tackling it. The campaign against tuberculosis cannot make any headway unless there are organizations for educating the people regarding the causes and ways of prevention of tuberculosis. This is one of the main functions of non-official organizations like the Tuberculosis Association of India and the State Tuberculosis Associations. The Association and its affiliates are aware of this and have taken steps to increase their activities in this direction. But they do not have the funds necessary to carry out all their programmes. A Tuberculosis Seals Sale Campaign is therefore being organized in the country for the first time in October this year and it is hoped that this will make the public more tuberculosis-conscious as well as bring in the necessary finance to increase its propaganda and other activities. This is one of the important and recognized methods by which National Tuberculosis Associations in other countries collect funds for their anti-tuberculosis work. To make this campaign a success, the co-operation of a large number of people in different parts of the country is necessary and this in itself will have a great educative value. The various tuberculosis associations, branches of the Red Cross Society and other voluntary organizations as well as individuals will be called upon to help in this campaign. The Association takes this opportunity to make a special appeal to all public-spirited individuals and

organizations to help the Tuberculosis Association of India in this new venture. It also appeals to the press in general, the cinema houses, the student population, the welfare organizations as well as industrial and labour organizations and social workers to assist in making this campaign a success. The money collected by this campaign will augment the resources not only of the central organization, but also of the State Associations.

TUBERCULOSIS SEALS SALE

STORY OF THE TUBERCULOSIS SEAL

A DANISH POSTMAN, while sorting out his unusually large mail during the Christmas season in 1903, thought of the tuberculous children limping across the road and wondered how these could be helped. He thought that if every letter or parcel carried an extra stamp in addition to the postage, the money realized from such stamps could be used for the cure of these sick children came to his mind. He talked this over with his fellow postmen and they agreed that they should try out an experiment whether money could be collected for tuberculosis work by this means. When they had a practicable scheme worked out, they submitted it to the King and Queen of Denmark who gave it their hearty approval. The first Tuberculosis Seals Sale was held during Christmas in 1904 in Denmark and this proved an unexpected success. In the first year the Danish people bought an average of two seals per person and from the proceeds they built the first big hospital for tuberculous children in Denmark.

Other countries took of a clue from the success of this venture in Denmark. The U.S.A. started a similar campaign in the year 1907. Since then the sale of Tuberculosis Seals during Christmas season increased year by year and in 1948 the National Tuberculosis Association of U.S.A. was able to collect 20 million dollars by this method. The sale of seals has since been adopted by Canada, U.K., and most of the countries in Europe, as well as Australia, New Zealand, etc.

OUR CAMPAIGN

The Tuberculosis Association of India has been considering for some time the question of using this method for augmenting its resources. Since its inception in 1939, the Association has made significant progress towards the stimulation and co-ordination of preventive and curative anti-tuberculosis measures in this country. What has been done, however, has only touched the fringe of the problem. The Association does not have at present the financial resources to carry out all its functions adequately. Due to war conditions and other considerations the Association could not organize any campaign till now to collect funds. Now the time has come for increasing the Association's activities and also to find the resources for this purpose and it has therefore been decided to start a Tuberculosis Seals Sale Campaign from this year. This campaign will serve not merely as a means of raising funds but also as a medium of health propaganda. The Stamps Sale in India is designed to give every individual an opportunity to contribute his or her mite to the anti-tuberculosis campaign. The money collected by this method will be used for the extension of the activities of both the Central and State Associations in different parts of the country.

The Tuberculosis Seal, which was originally conceived as a fund-raising device, has had a growing educational influence in matters concerning tuberculosis and health. Millions of people will get an opportunity to know something of the seriousness of the tuberculosis problem in India and also will have an opportunity to contribute their share to help to control it. Large numbers of

persons have to take part in this campaign. The control of tuberculosis thereby ceases to be the responsibility of the government or of a few individuals and it becomes a task of the people as a whole. The educational propaganda, preceding, during and after the actual sale of seals gives an opportunity to drive home to millions of people knowledge regarding the nature, prevention, treatment and other needs for the control of tuberculosis. The Tuberculosis Association of India requests all organizations and individuals to extend their full co-operation in making the Seal Sale Campaign a great success. It is scheduled to start on 1st October, 1950, and end with a Tuberculosis Week in January 1951. The Central Association will distribute to the State Associations stamps required by them for the campaign. The target for this year's campaign is the sale of one million sheets of 35 per stamps each. The Tuberculosis Association of India sincerely hopes that every individual in India will buy these stamps.

[We are unable to subscribe to this fashionable pessimism in tuberculosis and the consequent need of spending fortunes every year in combating the disease. As we have been showing by facts and figures for some time now, tuberculosis is a dying disease everywhere. The incidence in India compares very favourably with the one in England and Scotland. Our cattle have been known to be highly resistant, for over 50 years. Our laboratory animals are equally resistant. Is only man specially susceptible?

The measures that Indian experts are demanding now failed in England to check the spread of the disease some time ago. The settlement plans, like the Papworth Settlement, have definitely produced remarkable results. Children of tuberculous patients born and bred in the settlements have remained free from the disease. The ambitious plans of hospitals are not only expensive but also useless. In fact, they are harmful inasmuch as they come in the way of the settlement plans.

For details please see Editorials, vol. 83, Jan. 1949, p. 41 and vol. 85, June 1950, p. 261 and notes made from time to time as comments on original articles and medical news.—Editor, I.M.G.]

The following three items are reproduced from a Release dated 29th May, 1950, issued by Pan-American Sanitary Bureau, Regional Office, World Health Organization, 2001, Connecticut Avenue, N.W., Washington 8, D.C. :—

(1) SMALLPOX VACCINE

As stated earlier, the procurement programme of the Bureau covers a wide range. Another example is the case of several Latin American countries (Colombia, Ecuador and Peru) whose governments recently called upon the Bureau to assist them in their campaign against smallpox, which is endemic in several areas of Latin America. A difficult technical problem is involved in the campaign which these countries are carrying on, since the teams must reach inaccessible jungle and mountain areas, and smallpox vaccine is only useful for 90 days and must be maintained constantly in a near-freezing temperature. To make these campaigns really effective, the medical teams must, in some cases, go to areas in which there are no roads and which are only accessible by mule. In many of these areas there is no electricity; yet the teams must deliver the vaccine in a semi-frozen condition, within the necessary time limit.

Under the circumstances, the Bureau was faced with two possible solutions :

(1) The supplying of a newly-developed dry vaccine whose usefulness has not yet been proven in mass application, and which, moreover, is very expensive.

(2) The Bureau therefore is, for the time being, using a second solution as the more feasible, pending further improvements in the production of dry vaccine. It has sought from American industry assistance in supplying mobile refrigeration units capable of transporting the field teams, plus the vaccine which must be kept in a semi-frozen condition. These mobile units must also be capable of producing ten pounds of ice per day.

The Bureau is now arranging for provision of four-wheel-drive station wagons, on each of which is mounted a small refrigerator unit capable of producing the ten pounds of ice. It will also store the necessary vaccine. The refrigerator units will operate either from the car batteries or 110-volt or 220-volt plug-ins, for use where electricity is available. For areas beyond the reach of roads, the station wagons will be equipped with three-gallon thermos jugs, such as those used on picnics, in which will be stored the semi-frozen vaccine. This device, it is hoped, when perfected, will permit the operation of the teams for 24 hours beyond the use of roads, enabling them to reach practically all infected areas. Considerable headway is being made in the development of these mobile units, which should be ready for use within a few months.

The Bureau has already met many demands for smallpox vaccine from other areas of Latin America.

(2) DRUG FOR LEPROSY IN FAKFAK

Recently, the Dutch members of the U.N. Secretariat at Lake Success learned of the needs of a Dutch physician in charge of a leprosarium in Dutch New Guinea. The doctor had heard that a certain drug in tablet form had been developed in the United States for use against leprosy. In their desire to help this physician, they wrote to the PASB, asking if the Bureau knew of any such drug and where it might be purchased, to assist their fellow countrymen.

The Bureau informed them that such a drug did exist, that it was called diasonc, and quoted the price. The Dutch staff of the U.N. Secretariat made a collection among themselves of \$150.00 to cover the cost of the medicine and the expense involved for its delivery to Dutch New Guinea.

When the shipping instructions reached the Supply Section, it was found that the drug had to be sent to a location so isolated that it did not appear on any available map—a town called Fakfak, New Guinea. The PASB got in touch with the Dutch airlines and arranged for the delivery of the material by air to Biak, Dutch New Guinea. From there it was shipped on a copra boat to Fakfak. The Dutch physician in charge of the leprosarium has gratefully acknowledged receipt of the drug which he is now using with some success.

(3) TYPHUS VACCINE FOR AFGHANISTAN

Recently, a typhus epidemic broke out in Afghanistan. The government of that country made an urgent appeal for assistance to the World Health Organization Headquarters in Geneva, which passed on the request to its Regional Office for the Americas, the Pan-American Sanitary Bureau. Within 36 hours of the time W.H.O. received the request, anti-typhus vaccine left the United States by air for New Delhi, where the W.H.O. Regional Office arranged for its transportation by train to the end of the railway line at Peshawar in the Khyber Pass. From there it was transported by camel to Kabul.



Ka (3)

SAVE THE CHILDREN CONFERENCE

Delegates from 36 countries attended the meeting of the General Council of the International Union of Child Welfare which met recently in London. H.R.H. the Duchess of Kent talking to Mrs. Hanna Sen, Indian delegate, who represented the All-India Save the Children Committee at the Conference.



Kb. (10)

TELEVISING AN EYE OPERATION

Delegates to the 16th International Congress of Ophthalmology, held recently in London, were able to see delicate eye operations being performed at London hospitals with the aid of television. In the process the human eye was magnified to eight or nine times by the use of telephoto lenses. A white-clad camera operator operates the television camera while the operation (for a cataract) is carried out. Delegates in other rooms watched the operation.

TELEVISIONING EYE OPERATIONS

(Reproduced from Release No. B.F. 880 issued by British Information Services, New Delhi)

LIGHT-WEIGHT television equipment is being used at two London hospitals to unravel the 'secrets' of the eye for the benefit of the 1,200 delegates attending the 16th International Congress of Ophthalmology now being held in the British capital.

With the help of television, delicate eye operations can be watched by the delegates in large parties instead of having to take turns. From a special scaffolding built over the operating table, the television camera operator is able to follow every movement of the surgeon's hands.

The delegates can watch the operations from adjacent rooms, where telephoto lenses produce on screens close-up pictures, magnifying the human eye to nine or ten times the life-size.—L. P. S.

SEARCH FOR NEW SOURCE OF ANTI-ARTHRITIC DRUG

BRITISH EXPEDITION'S WORK IN W. AFRICA

By TREVOR I. WILLIAMS

Deputy Editor of the Scientific Journal 'Endeavour'
(Reproduced from Release No. B.F. 888 issued by British Information Services, New Delhi)

AN expedition which covered nearly 10,000 miles of West African territory has returned to London and issued a report which is likely to bring perceptibly nearer the conquest of rheumatoid arthritis.

The expedition was led by Dr. R. K. Callow, of the Medical Research Council, who was accompanied by Mr. R. D. Meikle, botanist from Kew Gardens, London. Their object was to discover plants which contain chemicals useful for the manufacture of cortisone, the remarkable new anti-arthritis drug, which is at present obtainable only from ox-bile, a source which makes the cost of treatment fabulously high. Such success has, however, been achieved with the new drug that a tremendous effort is being made by medical research workers all over the world to find some simpler source of supply.

COMPLEX OPERATIONS

The main reason for the present very high cost of cortisone is that ox-bile is not the direct source of the drug but merely a source of small quantities of raw material for its manufacture. Between the raw material and the finished drug are no less than 37 complex chemical operations in each of which, despite the greatest care, a proportion of the material is inevitably lost. The recent medical expedition arose from the discovery that certain species of African vine contain a chemical, sarmentogenin, which is much nearer to cortisone than ox-bile is. From sarmentogenin cortisone can be made in 17 operations instead of 37.

Important though it was, this new discovery created as well as removed difficulties. According to the scientific textbooks sarmentogenin was derived from the seeds of a West African vine known to botanists as '*Strophanthus sarmentosus*'. A Swiss expedition went out and brought back quantities of the seeds of this plant for chemical analysis. Unfortunately they proved to contain hardly any sarmentogenin—the botanical source of the all-important drug had been wrongly identified. All that was known was that the seeds from which sarmentogenin can be isolated are gathered by the local inhabitants and are occasionally put on the market in considerable quantities.

The purpose of Dr. Callow's expedition was to identify beyond doubt the plant from which the drug

had previously been extracted and to see what prospects there were of gathering the seeds in quantities sufficient for cortisone manufacture. The possibility of establishing plantations of the plant is being borne in mind.

DEADLY POISON

In the remoter parts of the country a primitive cultivation of '*Strophanthus*' is already practised—though it is not known yet whether it is of the sarmentogenin-producing variety—as the seeds also contain a deadly poison which the tribes use for tipping their arrows, in much the same way as the natives of South America use curare, another drug of great medical value. A secondary purpose of the expedition was to examine some of these poisons to see whether they have any practical value in the treatment of heart diseases and other complaints.

The expedition made its headquarters in University College, Ibadan, in Nigeria. Fortunately a scheme had already been launched for studying the properties of Nigerian plants and native medicines. In some places local rulers, alive to the possibility of new trade for their people, gave considerable help. The Emir of Katsina, for example, impressed the importance of the work so strongly on district and village heads that within four days more than 10,000 seed pods from the vine '*Strophanthus sarmentosus*' poured in, an embarrassingly large quantity for the small band of collectors to deal with.

The chemical analyses required to measure the quantity of sarmentogenin are too difficult to make with the limited facilities available in Nigeria, so the expedition transported its considerable collection of seeds, dried plants, and crude extracts back to London for detailed tests to be made. These are not yet completed, but there is an excellent chance that among them will be the plant which produces sarmentogenin. When it is found, there will be no difficulty in obtaining further supplies for Mr. Meikle, the botanist who accompanied the expedition, most carefully classified all the many plants of which specimens were brought back. This work will, incidentally, make a notable addition to the limited knowledge of the plants which grow in this part of the world.

INTENSIFIED RESEARCH

The expedition worked closely with the officers of the Agriculture and Forestry Departments in Nigeria and had an excellent opportunity of studying, if only superficially, the many medical and scientific problems in West Africa which demand attention. Although research has largely reduced the ravages of malaria in West Africa, the climate can be trying and local conditions are by no means ideal for scientific research. Nevertheless, a serious start has already been made at University College, Ibadan, and it is hoped that the intensified research which is now being made will result in the rapid extension of this.

From Nigeria science may bring far more than a new source of cortisone; it may bring many other important drugs from plants which have hitherto scarcely been examined, as well as effecting major improvements in agriculture and forestry.

[Reference may be made to the Editorial for the month of April 1950 for cortisone. Many species of *strophanthus* grow in India also.—EDITOR, I.M.G.]

27TH ALL-INDIA MEDICAL CONFERENCE

THE 27th All-India Medical Conference is going to be held in Sholapur on 26th, 27th and 28th of December 1950 when as usual the exhibition of medical and surgical products will be arranged. Those who intend to exhibit their products should immediately write to the Secretary, 27th All-India Medical Conference, P. O. Box 53, Sholapur.

Error of random sampling—0.025.

It is surprising to note that the largest number of incidence occurs in the very young age group of 5 to 10 years (18.8 per cent). That the next highest incidence (18.0 per cent) is in the age group of 25 to 30 years is not surprising because apparently healthy young persons are easily and readily affected. It is also noticed that the number of cases among the older age groups 45 to 60 are much fewer. It is surprising that even a partially breast-fed child of 2 years only was found affected. Its mother also suffered from the same disability. The significance of this observation has been discussed later. Sixty was found to be the maximum declared age of the examined persons. This does not necessarily mean that older persons are immune. Certainly it cannot be expected that illiterate and ignorant people would or could keep a correct count of their respective ages. Three score is indeed a very high and serviceable figure to them and might represent any age of 60 or higher.

Sex distribution.—In tables II and III the distribution of the cases by sex is given. It will be seen that 18 of the cases, *i.e.* 13.5 per cent of them, were women. This observation is in agreement with the reports of earlier observers that females were usually found to be less affected. Whether females are actually less susceptible to lathyrism or this observed lower rate of incidence is due to the natural shyness of Indian women to come forward for examination cannot be settled at the moment.

TABLE II

Distribution of 133 lathyrism cases by sex

Sex	Number	Per cent	REMARKS
Male ..	115	86.5	Distribution indifferent age group.
Female ..	18	13.5	In table III.

TABLE III

Age distribution of 18 female lathyrism cases

Age group	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60
Number ..	0	6	6	0	0	1	3	0	2	0	0	0
Per cent ..	0.0	33.3	33.3	0.0	0.0	5.6	16.7	0.0	11.1	0.0	0.0	0.0

It is interesting to note that not one case between the ages 15 and 25 was found. One of the explanations may be the unwillingness of the young married girls to come for examination.

Distribution by religion.—From table IV we see that out of 133 affected persons 102 were Hindus and 31 Muslims. This gives a percentage ratio of 76.7 to 23.3 respectively which is in close agreement with the proportional distribution of the two communities in the population. There is thus no evidence that either

community is more susceptible to the disease, although we are inclined to think, after considering all the known facts about lathyrism, that Muslims, as meat-eaters, would be more immune. But taking into account the fact that the disease usually occurs among the people in the lowest income group of the society, it is not surprising that the rate of incidence is a fair index of the proportional distribution of the two communities in the population. It is also important to remember that the Hindus (including Brahmins) of this locality are usually fish and meat-eaters.

TABLE IV

Distribution by religion of 133 lathyrism cases

Religion	Number	Per cent	REMARKS
Hindus ..	102	76.7	Proportional distribution is a fair index of the community ratio in population
Muslims ..	31	23.3	

Rate of incidence to overall population.—The total population of the villages from which the patients had collected at the examination centre is estimated at about 14,000. Even if it is assumed that all persons suffering from lathyrism had gathered, though this contingency never happens, the percentage of lathyrism cases becomes nearly 1.0. On the assumption that only a half of the cases assembled, the rate of incidence comes to about 2 per cent. This is indeed a very disturbing and distressing figure. Remembering the fact that most of the examined and affected persons (80 per cent) were fresh attacks of the year and that lathyrism means practically total disability (as far as man-power is concerned), an incidence of 1 or 2 per cent in each year represents a loss of man-power which will be continually on the upgrade as no cure from lathyrism has been discovered yet. Indeed,

Buchanan found as many as 13 per cent of some villages affected with epidemic spastic paralysis which is not surprising and which can be expected in other affected villages if a census is taken.

Discussion

Lathyrism is clinically diagnosed by the spasticity in the lower limbs, exaggerated reflexes, ankle clonus and Babinski's sign. Incontinence of urine and impotence are usually not in evidence although these symptoms may

be present in some cases. The disease is undoubtedly of nutritional origin and is, as pointed out before, essentially an economic one. Various theories about the aetiology of lathyrism have been advanced but none are entirely satisfactory or convincing.

Acton (1922), Anderson *et al.* (1925), Dilling (1920), Geiger *et al.* (1933), Jiménez Díaz *et al.* (1943), Howard *et al.* (1923), McCarrison and Krishnan (1934), Mellanby (1930), Rudra and Bhattacharya (1946), Shah (1939), Stockman (1934), Stockman and Johnston (1933), Stott (1930), Traland and Moharram (1932) and Young (1927) have all advanced hypotheses regarding the aetiology or refuted those of others. Vitamin A deficiency can produce nervous degeneration but so can vitamins B₁ and E deficiencies. In fact, Einharson and Ringsted have described motor nerve degeneration from deficiency of vitamin E. The degeneration of the central nervous system by vitamin B₁ deficiency and its cure by vitamin B₁ alone is so well known as to need no reference here. Wolbach has therefore cautioned against the acceptance of Mellanby's vitamin A deficiency theory, as not only can deficiencies of vitamins A, B₁, E and of other vitamins but sundry other causes also may bring about the degeneration. For example, Zimmerman and Burack (1934) observed nervous lesions in animals given sufficient vitamin A but deficient in the black tongue factor (nicotinic acid). The investigations of Professor Jiménez Díaz *et al.* (*loc. cit.*) have focused the importance of animal foods in the diet for preventing lathyrism. Bhattacharya working in the laboratory of Rudra isolated an albuminose-like substance from the *khesari* grains but it is unfortunate that the investigation could not be pursued further owing to its sudden termination.

It is now agreed that lathyrism can be and is produced by the exclusive or predominant use of *khesari* in the diet. This fact does not exclude the possibility of other grains producing the disease. Stockman (*loc. cit.*) claims that it can be produced by other pulses and even cereals. Geiger *et al.* (*loc. cit.*) reported that lathyrism had been induced in the white rat by feeding sweet pea (*Lathyrus odoratus*). Recently, Lewis *et al.* (1948) have produced experimental lathyrism in rats by feeding them sweet pea and certain species of *Lathyrus* peas other than *Lathyrus sativus*. Minchin (1940) reported cases in the Madras General Hospital which he concluded were lathyrism but doubted if these affected persons had had any *khesari* in their diets, as this pea is usually not grown in the area from which the patients came.

On interrogation all the affected persons examined replied that they had been subsisting on *khesari* for some time past. It should be remembered that when these people start taking this pea, they have exhausted their stock of all other grains and they consume practically only

this substance. They either cook the peas like rice or make them into *chapattis* with the pea meal and eat the rice or *chapattis* with *dal* made from the same grain. There is usually none of other foodstuffs. More than 80 per cent of the examined and affected persons were recent and fresh cases of from fifteen days to three months' duration. It is evident that most of the chronic cases had stayed at home although we had one or two of about ten years' duration.

Minchin (*loc. cit.*) quoting Basu *et al.* (1937) thinks it may be due to tryptophane deficiency. But Basu *et al.* have given no data or proof that *khesari* is deficient or how much deficient in tryptophane. Stockman (*loc. cit.*) thinks that lathyrism is caused by the toxic action of phytic acid and possibly other substances. Jiménez Díaz *et al.* (*loc. cit.*) reports that the *khesari* lacks in some vitamin-like substance which is present in foods of animal origin. This observation fits in very well with the results of investigations now being conducted in the senior author's laboratory. It has been found (Rudra and Chowdhury, 1950) that *khesari* is very poor in methionine content, having only about a quarter of the methionine content of most other *dals*.

It is very probable that the methionine deficiency with other multiple deficiencies present is really the aetiological factor of lathyrism. In the absence of adequate methionine in the diet a disturbance in the creatine metabolism may follow which may result in the degeneration of the nervous system specially of the pyramidal tract. The experiments of Bodian and Mellors (1947) in experimental neurone regeneration is interesting in this respect. The possibility of some toxic substance abetting the action of methionine deficiency is not altogether excluded.

We have already mentioned that a child of 2 years and practically breast-fed was also affected with lathyrism. The pertinent question then arises: Is the toxic principle transmitted from the mother to the child if the disease is of toxic origin? This is very much unlikely. For example, we cannot visualize the phytic acid taken by the mother being transmitted to the child through the milk. On the other hand, if the disease is actually a deficiency one like methionine deficiency, the child's illness can be explained. Since the mother's diet was very poor in methionine content, her milk would also be poor in methionine and, although the child was taking milk, it was continually being deprived of this essential amino acid.

We have also observed that fewer female cases are usually found. Are females less susceptible? We cannot settle this question here and now. But if a disturbance in the creatine metabolism is the real cause of lathyrism, we will not be surprised if females are actually found more resistant to the disease

McCarrison and Krishnan (*loc. cit.*) found no female cases in the Gilgit agency. It is probable that his investigation was not exhaustive.

Cruickshank (1947) described a similar spastic syndrome among European prisoners of war in the military camp at Singapore occurring first in September 1942. This most probably happened on account of the very poor diet of the prisoners lacking in calories, proteins, fats, minerals and vitamins. Treatment with good, nutritious and balanced diet and adequate vitaminization gradually altered the patients' conditions but there was no total cure as in lathyrism. Jacoby (1947) reports that in Bhopal lathyrism usually occurs during or after the rainy season and once the disease has affected, the condition of the patient continues to deteriorate even if the diet consists of 50 per cent of wheat. He further suggests that the disease may be due to fungus growth on the Lathyrus grains because of bad storage condition during the rainy season.

Suggestions

The best treatment that we can recommend from our present knowledge is an all-round improvement in diet rather than medication. We appreciate that this is rather a tall order and extremely difficult of realization in the present economic state and food supply position of the country. Jacoby (1946), we think, was first in introducing prostigmin in the treatment of lathyrism.

With a generous gift from the manufacturers, the Roche firm, one of us (M. N. R.) with H. C. Ghosh had the opportunity of testing the efficacy of this drug in lathyrism. We must confess that in our experience prostigmin does not promise to be a remedy for lathyrism. There have been some improvements in some cases, no doubt, and in our opinion it can be used for relieving some of the signs and symptoms. The biochemistry of lathyrism is now being investigated in the laboratory of one of us (M. N. R.).

We must also emphasize the rôle that the plant geneticist has to play in this connection. An alternative crop must be evolved which will be as hardy and cheap as *khesari* and still have a nutritive value equal to that of the best of our pulses.

We offer our best thanks to Lieut.-Colonel H. J. Curran, I.M.S., lately Principal and Superintendent, Darbhanga Medical College and Hospital, for his keen interest in this investigation.

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THE RISK OF POLLUTION OF GROUND WATER FROM BOREHOLE LATRINES

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and

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Two important problems in rural sanitation in India are the collection and safe disposal of human excreta and the provision of safe water supplies which cannot be contaminated by human excreta. The two are to a certain extent interrelated. Villagers, as a rule, have no latrines for defecation. They pollute the soil, wash themselves in rivers and tanks and use them as sources of drinking water also.

The provision in every house of a borehole latrine or pit latrine where ablution will also be carried out and the construction of properly conserved wells for drinking water are advocated as the solution to the problem. Borehole or pit latrines do not require any handling of night-soil for disposal. They are cheap and can be made fly-proof and free from the risk of hook-worm propagation if certain details are taken care of. Many such latrines have been built in different parts of the world in rural areas.

The borehole latrine consists of a hole 14 inches to 16 inches in diameter dug in soft soil so as to penetrate about 3 feet into the subsoil water. A sanitary latrine seat is placed on the surface with suitable arrangements for privacy. The excreta undergo anaerobic digestion in the hole. Even if the borehole did not penetrate the subsoil water, excreta deposited would undergo digestion either aerobic or anaerobic or both, according to the environment.

Public health workers have entertained doubts about the wisdom of encouraging such self-disposing latrines and leaching cess pits in rural

areas on account of the risks of bacterial pollution of ground water in the wells used as sources of drinking water.

The extent of pollution diffusing from a borehole latrine into the ground water has been studied by several workers through a number of detailed experiments. Their results are briefly summarized in the table and have also been plotted in the graph.

The graph suggests that the extent of travel of pollution from a borehole (or a leaching cess pit) into the ground water appears to depend mainly on the velocity of flow of ground water. This velocity will depend largely on the mechanical structure of soil. The finer the soil and the smaller its effective size, the greater will be the frictional resistance to flow of water, the lower will be its permeability coefficient. The velocity will depend also upon the gradient of the water-table, according to D'Arcy's law. The hydraulic gradient will depend on the head (or the draw-down in the case of a well from which water is pumped). From the graph it appears as if the travel of bacterial pollution in subsoil water is not more than the distance covered by

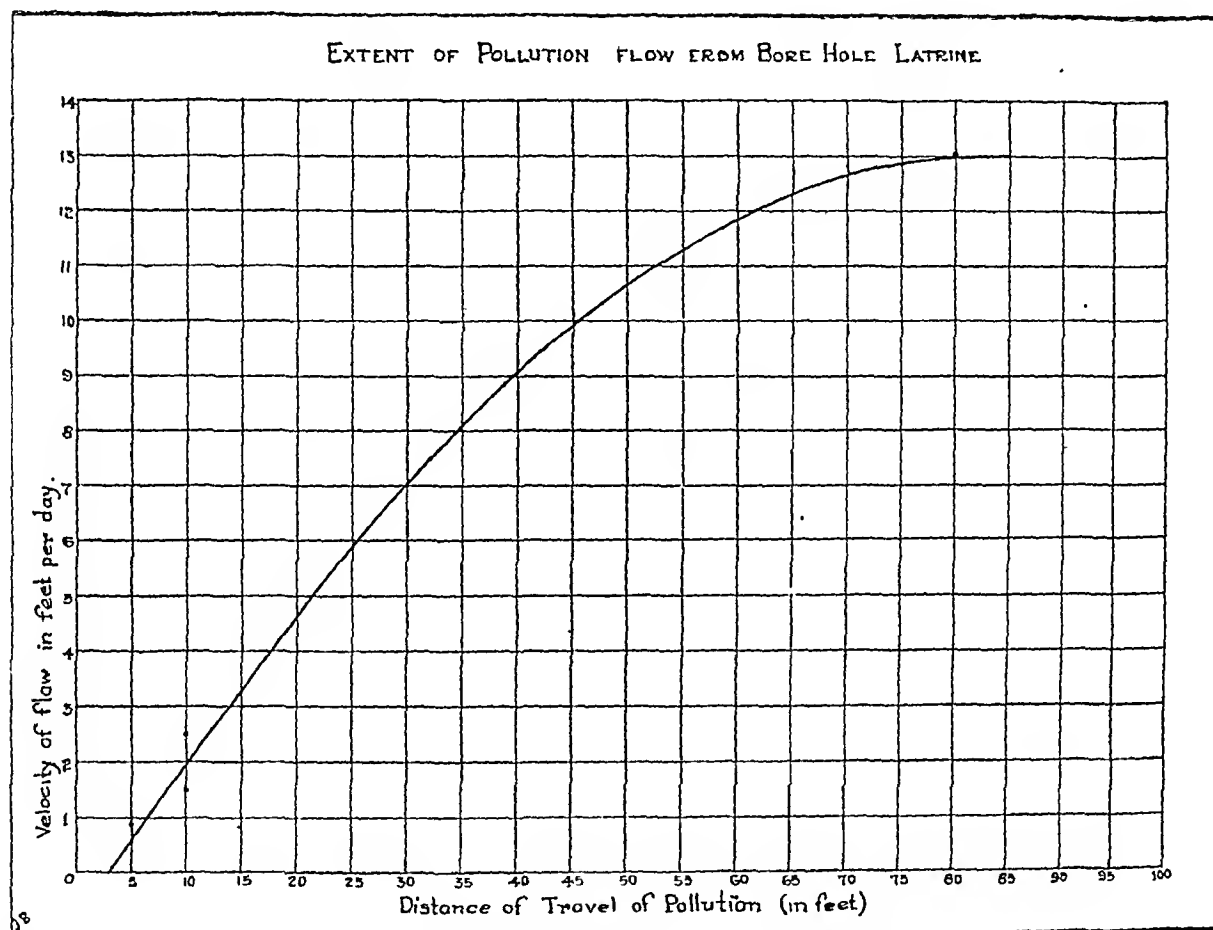
TABLE
Pollution flow from borehole latrines under different soil conditions

Nature of soil	Place of experiment	Investigators	MECHANICAL COMPOSITION OF SOIL IN THE REGION OF WATER FLOW			GROUND WATER CONDITIONS			Maximum distance of <i>B. coli</i> flow in ft. (observed)
			Average content of sand and fine gravel (per cent)	Region of coarsest soil		Water-table range in ft.	Velocity flow in ft. per day	Slope of water-table (in 100 ft.)	
				Effective size* (mm.)	Uniformity co-efficient				
Permeable soils under the latrine boring.	Model town : Lahore, Punjab, India.	Brian R. Dyer (1941).	..	0.10	1	..	5
	Singur, Bengal, India.	Brian R. Dyer and T. R. Bhaskaran (1945).	90	0.20	2.0	3-13	2-3	0.5 to nil	10
	Covington Country, Alabama, U.S.A.	Elfreda L. Caldwell and L. W. Parr (1937).	92	0.12	2.7	3-9	1-2	0.16-0.27	10
Impervious stratum closely underlying latrine boring.	Wingard Experimental Station, Alabama, U.S.A.	Elfreda L. Caldwell (1938).	92	0.13	5.2	8-12	8	1.36-2.83	35
	Wingard Experimental Station, Alabama, U.S.A.	Elfreda L. Caldwell (1938).	93	0.17	2.3	5.7	13	1.8-2.5 and 5.9-9.7	80

the ground water in 4 to 7 days. It is possible that coliform organisms do not survive more than 4 to 7 days in the anaerobic environment in which ground water travels. It has also been observed that the distance to which pollution travels from a borehole latrine gets reduced after a few weeks when a gelatinous membrane is established on the soil particles and acts as a barrier to the travel of bacteria. This is the condition in which the soil becomes a real filter comparable to a sand-filter filtering water.

rock, limestone or gravel, the actual velocity of flow of ground water may be high and the distance between a borehole latrine and a well may have to be increased correspondingly. But in the plains, where the subsoil water-table may have a slope of less than 1 in 100 and the soil is fine sand (effective size* not greater than 0.25 mm.), the ground water velocity will not exceed 3 feet per day, and a horizontal distance of 25 feet will be ample as a margin of safety against pollution.

GRAPH



Hence the safe distance between a borehole latrine or leaching cess pit and a ground water source may be taken to be the distance represented by about 8 days' travel of the ground water. If and when the gelatinous membrane of defence is formed in the soil around the borehole, there will be a mechanical barrier to arrest bacteria, and the factor of safety will be increased.

In the case of rural wells or tube-wells, the maximum rate of draw from the well is likely to be about 400 gallons an hour. At a horizontal distance of 20 feet from the well, water may flow only with velocity of 2 feet per day through a stratum 6 feet thick. A distance of 25 feet may provide sufficient margin of safety in such circumstances.

If the soil is fissured, or spongy or contains large voids, as in the case of badly shattered

An examination of the soil and observation of the ground water velocity or gradient would be helpful in determining the safe distance where there is a doubt.

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* The 'Effective Size' of sand is the diameter of sieve opening such that 10 per cent of the particles by weight are small enough to pass through it, and 90 per cent will be retained on it.

The Indian Medical Gazette Fifty Years Ago

LONDON LETTER

(From the *Indian Medical Gazette*, September 1900, Vol. 35, p. 360)

War Hospital Scandal

SUCH is the formula which, during the last week, has taken the most prominent position in the posters which announce the contents of the daily papers. It is a rude awakening. Up to then the British public had been living in a fool's paradise, comforting itself with the belief that whatever mistakes have been made in the prosecution of the South African War two departments, the Army Service Corps and the Royal Army Medical Corps, have rendered admirable and effective service and performed the important work of ministering to the sustenance of the army and the relief of the sick and wounded as well as under the circumstances of the campaign it could possibly be done. Mr. Burdett-Coutts, M.P. for Westminster, best known as the husband of the aged and philanthropic Baroness Burdett-Coutts, is responsible for having opened the eyes of the public and presented pictures of neglect and suffering which have shocked the nation and touched the hearts of people who have relatives and friends at the front—and their name is legion—on the tenderest spot. Mr. Burdett-Coutts' revelations appeared in the *Times*.

Accredited by that paper, which has since the commencement of the war had a severely critical eye on the hospitals, he proceeded to South Africa, and made it his business to observe the treatment of the sick and wounded. Among other places visited by this gentleman was Bloemfontein and this visit took place at a time when the resources of the medical department were strained almost to breaking by the severe outbreak of enteric fever which occurred after Lord Roberts' celebrated march, and in consequence of the conditions encountered during that arduous operation. There can be no doubt that the incidents and scenes described by Mr. Burdett-Coutts were actually witnessed and truly described by him. The fever-stricken, numerous beyond all reasonable anticipation, had to be accommodated and treated in the field hospitals and tents, and for a time attendants and appliances were insufficient and perhaps inefficient. The matter is to become the subject of special enquiry, and a final judgment on the merits of Mr. Burdett-Coutts' accusations must

be suspended. The questions that arise are—Was there reason to anticipate so sudden and extensive an outbreak of enteric fever? Could arrangements have been made under the circumstances to meet the contingency? Were agents and appliances forthcoming in sufficient abundance and of proper quality to grapple with the emergency when it did arise? If default existed was that the outcome of a faulty system or the result of culpable error or shortcoming of any department, authority or individual? Mr. Burdett-Coutts is careful to acquit Lord Roberts and officers of the Royal Army Medical Corps of blame in the matter, and throws the onus of failure on the system which, he contends, is too much bound and fettered by red-tape and not devised upon sufficiently generous and progressive lines, more especially as regards skilled nursing and comforts.

War is War

This is practically the apology of the War Office for the hardships which the sick and wounded have had to sustain. Suffering is inevitable in war, more especially during operations such as those which Lord Roberts conducted when he advanced rapidly on two occasions into the heart of a hostile country—taking risks which subjected his army to unavoidable exposure, to influences and conditions imperilling health and life, banishing comfort and excluding the amenities and humanities of ordinary existence justifiable only by compulsion and success.

The loss of health and life and the hardship and suffering sustained were the price paid for the success attained and this was substantial and undoubted. But apart from this view which, though sound enough, is of an *à priori* character, apologists who have had equal opportunities of observation, and equal, if not superior, power of judging have come forward to testify that in this war, which, we may reasonably hope, is now nearly ended, the medical department official and non-official has acquitted itself admirably and done all that could be done to succour the sick and wounded. Sir William MacCormac, Mr. Treves, Sir William Stokes and many other medical men who have been intimately concerned in the management of hospitals and treatment of those disabled by disease and injury have given strong and warm evidence to this effect. The results of treatment are also very favourably represented by the case mortality of diseases and wounds. It would be absurd to deny that the experience gained in this war has not revealed defects and suggested improvements, and good will undoubtedly come of a searching inquiry if judiciously conducted by competent persons.

Current Topics, Etc.

Meteorites Bring News from Space

By MAURICE GOLDSMITH

UNESCO Science Editor

(Reproduced from UNESCO Features, No. 27, 15th August, 1950, page 12)

THE biggest meteorite crater in the world has just been discovered in the barren lands of Ungava, in Canada's Northern Quebec. From a study of this and the region above the earth's surface whence it came, we shall obtain more information which will eventually help us to invade and travel in inter-planetary space.

The existence of the crater is reported by a scientific expedition organized by the Royal Ontario Museum of Geology and Mineralogy, led by its director Dr. V. Ben Meen.

A crater helps us to find out what is happening in outer space. It is blasted out of the hard earth by a meteorite, which is a cosmic bullet come to earth. Those cosmic bullets that do not fall on land are known as meteors. You can see them on any clear moonless night darting across the sky in the form of flashes of light. It is estimated that about 5,000 millions of them enter the earth's atmosphere every day. Only a few of them fall to earth. When they do they cause great destruction.

The Canadian crater is a gaping wound on the face of the earth. It has a rim of about seven and a half miles' circumference and is two and a half miles wide. Hewn of solid granite, and containing a small lake in the centre.

Dr. Meen's view is that the meteorite was of tremendous size. If a similar meteorite were to strike a modern city, the city would be torn from the earth and life would be eliminated within a radius of 100 miles by the shock waves. The crust of the earth would ripple like pond-water.

But, he guesses, this gigantic cosmic collision took place between 3,000 and 5,000 years ago. The only living persons known to have seen a meteorite hit the earth are the inhabitants of the Siberian village of Novopokrovka, a few hundred miles from Vladivostok. It was at 10.35 in the morning, just three and a half years ago when, 'started by a brilliant flash like a bolt of lightning from the sky', children from the local village school hurried out of doors. 'In the sky overhead, they saw only a long dark streak. The strange track hung in the sky for many hours, and when darkness fell, it glowed like a streamer of the northern lights, against a background of sky that was itself unusually luminous.

'Hundreds of other people in the same area who happened to be out of doors got a direct look at the phenomenon. Against the blue of the sky they saw a ball of light as brilliant as the sun and about the size of the full moon. It travelled across the sky towards the south, shedding showers of sparks and carrying in its immediate wake a brightly coloured track which quickly turned into a thick black trail. Within four or five seconds, the object had disappeared in the general direction of the Sikhotaalin Mountains of Eastern Siberia.' (This is the description given by Dr. Otto Struve, Professor of Astronomy at the University of California, in the *Scientific American* for June 1950.)

A scientific expedition from Moscow investigated the region where the meteorite had fallen and found a

series of more than 100 holes, some of them 30 to 40 feet deep and as wide as 75 feet at the top, scattered over an area of one square mile. All around they saw destruction caused by what they describe as a 'rain of iron'. The rocks had been shattered. The trees had been felled, and some had been up-rooted and thrown several miles high in the air. The ground was strewn with pieces of meteoritic iron ranging in weight from several hundred pounds to tiny specks. It was estimated that the meteorite originally must have weighed about 1,000 tons and had a diameter of some 30 feet.

In Arizona, there is the relic of a similar destruction by a meteorite which occurred in pre-historic times. There is a single huge hole in the ground about a mile across and several hundred feet deep.

On the average, visible meteors are only 40 to 80 miles above the earth's surface and their light and heat result from friction with the air. They are related to comets and to the cosmic dust clouds of the Milky Way. A meteor makes those bright flashes we see because of the speed at which it travels. When it enters our upper air, it may be moving about 25 miles a second. The further it falls, the more resistant the air becomes and the meteor is slowed down by the atmospheric friction. Whether or not the meteor will disappear in the air depends upon its size. The smaller ones do because their surfaces become greatly heated, they liquefy and become entirely vaporized. The meteorite, however, hits the earth because its mass has been large enough to withstand this process.

The study of the slowing down of meteors in the upper atmosphere has become of importance in recent years with the development of new techniques. With these, for example, it is possible to get an idea of the temperature of the upper air. It has been discovered that it is much hotter, 40 miles up than at the earth's surface—a surprising fact, in view of the sub-zero temperatures in the stratosphere.

The newly discovered meteorite crater in Canada and the smaller one in Siberia are natural phenomena resulting from events remote from us in space and in time. Yet, as Dr. Harlow Shapley, world-famed director of the Harvard College Observatory, says, 'they are going to give us accurate information on the temperatures, densities and other properties of the earth's surface at 40 to 80 miles above the earth's surface.

'And precise information on this region of the atmosphere is exactly what we need for the development of high altitude jet-propelled airplanes, as well as for the rocket ships of the near future. The part of the earth's gaseous envelope that was formerly reserved wholly for the shooting stars has now become a region invaded by ambitious man, who no longer finds himself confined to the earth's surface and to the thick cloud-travelled lower atmosphere. He wants high-altitude wings and the meteors can help in their design and use.'

Nutritional Megaloblastic Anæmia : So-called Pernicious Anæmia of Pregnancy

By B. V. KOTHARI
and

Y. M. BHENDE

(Abstracted from the *Indian Journal of Medical Research*, Vol. 37, July 1949, p. 347)

A PRELIMINARY report of 40 cases of so-called pernicious anæmia of pregnancy is submitted.

A detailed analysis of these cases shows that no symptoms are specific and no physical signs diagnostic

for this anaemia. The only reliable criteria for the diagnosis of this condition are: (i) the presence of a true megaloblast in the peripheral blood and (ii) the presence of a true megaloblast in the marrow.

These criteria, originally laid down by Callender for the pernicious anaemia of pregnancy as met with in the temperate climate, are applicable to the similar condition seen in this country.

It is argued that clinically, haematologically, and aetiological, the pernicious anaemia of pregnancy as met with in the West is identical with the similar condition met with in India and the tropics.

A new term *nutritional megaloblastic anaemia* is proposed for this anaemia. It is pointed out that this anaemia can also be encountered in non-pregnant females and males of any age.

The importance of a full haematological investigation in every case of anaemia is stressed.

Treatment of Typhoid Fever with Bacteriophage

By R. G. DHAYAGUDE

and

D. D. BANKER

(Abstracted from the *Indian Journal of Medical Research*, Vol. 37, July 1949, p. 249)

RESULTS of treatment of 24 cases of typhoid fever with an unselected stock bacteriophage (later found to be an 'O' phage) are presented. Of these, 10 were treated by the oral route, and 14 by the intravenous route. Alternate patients were kept as controls, enabling a valid evaluation of the therapy. *S. typhi* was isolated from blood-culture in each patient before treatment.

The results of intravenous phage therapy appear to be sufficiently promising to warrant further trial with type-specific Vi phage, either alone or pooled with an 'O' phage.

Penicillin and Black Hairy Tongue

By W. E. OVERMAN

(From the *Journal of the American Medical Association*, Vol. 141, 31st December, 1949, p. 1319)

I SHOULD like to report another case of black hairy tongue which apparently resulted from oral administration of penicillin troches. Mrs. H. H. D., age 58, was seen on 21st October, 1949, with a chief complaint of sore throat and feverishness for forty-eight hours. The physical examination revealed moderate pharyngitis and oral temperature of 100°F. but no other significant physical findings.

Medication consisted of penicillin troches, 50,000 units every three hours during waking hours, and acetylsalicylic acid, 1 tablet when required for discomfort. Three days later, after having taken 18 troches, the patient returned for check-up. The throat and temperature were normal. The tongue was noted to be normal in colour. Six days later, the patient stated by telephone that after her previous return visit, sore throat had again developed and that she had purchased 24 penicillin troches and had used them according to previous directions. After having taken half the

troches, she noted a black discoloration of the tongue almost to the anterior tip. Twenty-four hours later (she was still taking penicillin troches) she noted that the tongue was black to the tip. She consulted me the following day. The tongue was found to be brownish black with hairlike projections over the visible portion of the dorsum of the tongue. Penicillin therapy was discontinued. One week later there was some clearing of the tongue. At this writing the tongue has almost completely cleared. No medication has been given since discontinuation of the penicillin troches.

Air-Cooled Buildings and Electric Fans

(From the *Journal of the American Medical Association*, Vol. 141, 31st December, 1949, p. 1329)

IN hot weather when the skin and clothes are wet with perspiration, the cooling of buildings to 80°F. is more dangerous in chilling some persons than is the use of the fans without artificial air-cooling. Experiments have shown that when subjects enter a space cooled to 80°F. with 50 per cent relative humidity from the hot out-of-doors (95°F. with 40 per cent relative humidity) the loss of body heat momentarily increases to a rate that is from five to ten times greater than the normal metabolic rate. In persons who are sensitive to cold, the peripheral vasoconstriction produced during the initial chilling period may persist for hours with shivering and discomfort.

A fan can cool only those body areas exposed to the wind and only by evaporation of sweat, since there is practically no heat loss by radiation and convection at 95°F. regardless of air velocity. The initial local chilling may produce vasoconstriction over the entire superficial area and reduction of sweating. Sooner or later, however, secondary vasodilatation will set in with a feeling of warmth, due to accumulation of metabolic heat in the body. A fan cannot give much relief from the heat under these conditions, regardless of current velocity. Moreover, too high velocities are enervating and unpleasant to most persons.

It is therefore obvious that, in the absence of body chilling, air cooling is a much more effective method of promoting comfort in hot weather than is the use of fans and that neither method is dangerous when chilling can be avoided.

Extract of Wings of Philippine Butterfly, *Terias hecabe* Linnaeus, New Antibiotic for Malaria

By E. Y. GARCIA

(From the *Philippine Medical Association Journal*, Vol. 25, June 1949, p. 279, as abstracted in the *Journal of the American Medical Association*, Vol. 142, 7th January, 1950, p. 63)

GARCIA cites evidence to the effect that para-aminobenzoic acid is essential for the growth of malarial parasites and reasons that the presence of any substance capable of inhibiting the action of this acid can disturb the growth of the plasmodia. The antimalarial effect of sulphonamide drugs, for instance, seems to be due to its antagonistic action toward para-aminobenzoic acid. The action of sulphonamide drugs is indirect or antibiotic rather than parasitocidal. The author tried 'hecabepterin', a pure extract of the wings of the Philippine butterfly (*Terias hecabe* Linnaeus), on

malaria patients. After preliminary trials, which indicated that a more concentrated extract of hecabepterin was necessary, Garcia describes observations which indicate that the para-aminobenzoic acid was either destroyed or inhibited by the extract, resulting in the disappearance of the erythrocytic parasites. This treatment was tried on 30 human subjects, selected for having had relapsed infections. These subjects included 16 with infection caused by *Plasmodium vivax*, 10 with *Plasmodium falciparum* infection and 4 with *Plasmodium malariae* infection. The average rates of decrease in parasite counts in infections with *P. vivax* and *P. malariae* were 52 and 45 per cent respectively, compared with their corresponding controls, while that in infection with *P. falciparum* was 74 per cent that of its control. Apparently the extract of butterfly wings, hecabepterin, exerts an antibiotic effect on malarial parasites. This is the first time in this age of antibiotic therapy for bacterial organisms that an antibiotic has been found for a haemoprotozoan parasite. The insect world seems to be another possible source of antibiotics for bacteria and protozoa.

Pertussis Treated with Chloramphenicol

By E. H. PAYNE *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 141, 31st December, 1949, p. 1298)

CHLORAMPHENICOL (chloromycetin) is effective in the treatment of pertussis.

When the antibiotic is administered as a rectal suppository or intravenously, the results are equal to those with oral medication.

Untoward reactions to chloramphenicol appear to be negligible.

Control of Biological Warfare

(From the *British Medical Journal*, i, 14th January, 1950, p. 112)

DURING the last three weeks the world has received two reminders that the effective control of atomic weapons, even if this could be achieved, would still leave equally unpleasant alternative methods of human destruction. Mr. Trygve Lie, United Nations Secretary-General, deplored that the Atomic Energy Commission, which was entrusted with preparing proposals for the elimination of all weapons of mass destruction, had never discussed biological and chemical warfare. And on Christmas Day the trial opened in the Soviet Far East of twelve senior Japanese officers accused of preparing bacteriological warfare against Russia. According to the indictment, a research station with a staff of about 3,000 was constructed in secret in Manchuria during 1936, and large-scale production was started of the organisms of bubonic plague, typhus, anthrax, and cholera. Fleas were bred in 4,500 incubators, and an apparently successful epidemic of plague was produced experimentally in Southern China in 1941 and 1942. One of the accused, a general in the Japanese Army, gave details of the type of weapons that were designed to spread the organisms. These included small sprays fitted into walking sticks and fountain pens, but the main agents were to be porcelain bombs dropped from aircraft. American, Chinese, and Russian prisoners of war are reported to have been experimentally infected.

Before the war it was known in Britain that Germany was conducting experiments in bacteriological warfare.

and an organization was set up to consider counter-measures. A few months after the Japanese surrender, it was disclosed that Britain, the United States, and Canada had been co-operating in energetic research on biological warfare since 1942. The project was an ambitious one—almost 4,000 people were employed for this purpose by the United States Army alone. Among the achievements were the development of methods for the mass-production of organisms and their products, and the isolation and preparation for the first time of a crystalline bacterial toxin. Means were discovered for the rapid and accurate detection of minute quantities of disease-producing agents for the manufacture of effective toxoid on a large scale, and for protecting clothing and equipment from infection. The attitude of this country to the investigations was clearly defined by the War Cabinet in 1942: 'That our principal aim in these studies and experiments was defensive and protective, and that we should, under no circumstances, initiate these forms of frightfulness.'

Mr. George W. Merck, United States Government Consultant for Biological Warfare, emphasized in his report of 1946 that the limits of biological attack had by no means been completely measured; and that, unlike the development of atomic energy, the production of effective agents for such warfare was possible without vast expenditure of money or the construction of large factories, and under the guise of legitimate bacteriological research. As pointed out in a leading article in the *Journal*, the technical difficulties of an international control of preparations for biological warfare are so considerable as to make efficient supervision impossible at present. The potentialities of such attack are so great, however, that its prevention deserves some thought even by an organization obsessed with the atomic bomb.

Cyprus Freed from Malaria Successful Campaign

(Abstracted from the *British Medical Journal*, i, 14th January, 1950, p. 119)

THE Secretary of State for the Colonies, Mr. Arthur Creech Jones, M.P., addressed a press conference on 9th January at which he announced the successful conclusion of the three years' anopheles eradication campaign in Cyprus. When the campaign started there were 18,000 cases of malaria annually in Cyprus, which has a population of 456,000 and an area of 3,500 square miles. It was said that 70 per cent of village children had malarial parasites in their blood. The number of cases on the island was reduced to about 100 last year, none of them new infections. Infant mortality, largely due to malaria, had dropped during the last seven years from 180 per 1,000 live-births to fewer than 70.

Mr. Creech Jones introduced Mr. Aziz, C.B.E., Chief Health Inspector of the island, and three Cypriots, members of the eradication team, which numbered 770 at the peak of the campaign. Mr. Aziz, who had originally studied under Sir Ronald Ross, was sent to Egypt in the early part of the war to study eradication methods there, and on his return introduced into Cyprus a system which depended mainly upon spraying and the use of D.D.T. The three anophelene species which had to be combated were *A. superpictus*, breeding in shallow collections of water exposed to full sunlight; *A. clitus*, breeding in marshy collections of water; and *A. bifurcatus*, breeding in heavily shaded water and in caves and wells.

The first of the vectors was attacked in 1946 over an area of 500 square miles in the region of the Karpas peninsula, and the attack was highly successful, whereupon the campaign was extended to the whole

island and against all three carriers. The attack was made with insecticides and larvicides, usually 4 per cent D.D.T. in gas or fuel oil. Gammexane smoke was issued in buildings with high ceilings and in places difficult of access. The spraying was carried out with locally made or imported 'fit guns', and all the work was checked repeatedly by special squads.

The campaign, which cost under £300,000, or about 13s. per head of population, was financed by the Government of Cyprus, apart from an initial grant of £17,000 from the Colonial Development and Welfare Fund. Cyprus can now be declared free of malaria-carrying mosquitoes, and a constant watch is maintained against reintroduction by ships or aircraft.

Recent Advances in the Study of Venereal Disease

By J. E. MOORE

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. 42, August 1949, p. 629)

This communication is a report of recent American advances in venereal disease research.

The prophylaxis of gonorrhoea.—Two United States Navy studies have shown that penicillin, orally administered, is of value in the prophylaxis of gonorrhoea. A single oral dose of 0.2 to 0.25 mega units, administered two to fifteen hours after potentially infectious exposure, reduces the incidence of gonorrhoea two to twelve-fold from that in a control group.

Aureomycin, orally administered, is of value in the treatment of gonorrhoea.

The penicillin therapy of syphilis.—The advent of procaine penicillin has raised the possibility of the cure of early syphilis with a single injection of the drug. Procaine penicillin is a highly insoluble salt. When suspended in oil plus 2 per cent aluminum monostearate, a single intramuscular injection of 0.6-1.2 mega units provides a measurable blood level (0.03 u/cc.) for five to seven days. When this drug is administered in a single dose of 0.6-0.9 mega units to persons exposed to infectious syphilis, the incidence of development of early syphilis is reduced from about 60 per cent (in a control of untreated series) to about 5 per cent. This is a practical application of abortive early treatment, based on the facts that in any infection, penicillin dosage may be reduced in proportion to the age of the infection and the number of infecting organisms.

Failure rates in early syphilis in relation to serologic pattern.—An elaborate clinical and serologic study has shown that in early syphilis, clinical outcome measured in terms of early relapse, within the first three to four years, is closely related to type of serologic response.

Pre-natal syphilis.—Further experience confirms the fact that penicillin is far superior to any other method of treatment in the prevention of pre-natal syphilis, the failure rate in terms of syphilitic infants remaining at 1 to 2 per cent. It has also been shown that if 'adequate' metal chemotherapy or penicillin has been administered to syphilitic woman, re-treatment during every subsequent pregnancy is not necessary. These facts are of major public health importance.

The Jansch-Herzheimer reaction.—In both early and late (especially neurosyphilis) infections, the febrile response following the initial dose of penicillin is an all-or-none phenomenon, which does not occur with doses of 10 u/kg. or less; but does occur with equal frequency and severity with a larger dose of any amount. From the practical point of view, the reaction

cannot be avoided by the initiation of treatment with small doses. Clinically, the reaction is not troublesome except in general paresis of the insane, where it may be serious.

The Management of Acne in General Practice

By H. W. JOLLY

and

M. E. KOPFLER

(Abstracted from the *New Orleans Medical and Surgical Journal*, Vol. 102, December 1949, p. 312)

In acne vulgaris, as in any other disease of really unknown or multifactorial aetiology, treatment cannot be classified as specific and non-specific or supportive. Therefore, we shall not impose upon you 'our' treatment and close the discussion of other therapeutic phases. Instead, we shall discuss all suggested phases of therapy endeavouring to bring them up to date and help to evaluate them in our opinion.

Therapeutic agents and classes may be grouped as follows:—

A. Psychological

It is quite satisfying to note the change in many persons' personalities paralleling the improvement of their acne. There arises also the psychosomatic question. Mitchell Heggs states acne often produces an inferiority complex, later an anxiety state. Some writers state the reverse is true.

At any rate the patient should be treated from a psychological view-point. Untold psychic trauma has been dealt with many patients by telling them not to worry, their skin will clear up with age. These patients should be reassured to place their minds at rest should there be a psychic aetiological factor, and secondly, to assure their co-operation for the long treatment period ahead.

B. Constitutional

The general patient should of course receive attention, not just the presenting complaint. Rest, anaemia, foci of infection, constipation, and intestinal parasites should be considered and investigated. Some authors stress some, minimize others. Osborne minimizes the rôle of constipation, Miller suggests control of this complaint by diet and exercise. Habits of traumatizing the face with the nails and fingers should be strongly discouraged. It is a fairly common observation to see the right side of the face markedly more severe than the left, merely because most people being right-handed, that side of the face is more 'accessible'.

C. Local therapy

1. *Topical.*—This undoubtedly is the most frequently used and abused form of therapy. Strong or irritating preparations are neither necessary nor beneficial. Since the overwhelming majority of patients suffer from excess oiliness, a removal of these oils is indicated. Klauder recommends soap, water and alcohol. Swartz and Blank report the use of a detergent composed of 25 per cent sulphated oil (emulsifying agent), 25 per cent mineral oil, and 50 per cent water, as a cleansing agent used in 400 patients with good clinical results. They recommend its use three times daily on an unmoistened skin and removal with warm water.

Soap and water seem adequate in most cases as a cleansing agent. However, it must be borne in mind that many skins are chapped from over-drying by soaps,

in which case its use must be decreased or some milder soaps used. Strong or medicated soaps are not advisable.

Keratolytic ointments and sulphur ointments or their combinations are still in wide use and are often beneficial if judiciously used. New preparations combining these medicaments have appeared in wetting agents and cosmetic bases. It seems questionable how much the efficacy of these drugs has been increased thereby.

2. *Surgical*.—Some surgical procedures become indicated in almost all cases. We believe they should be minimized as much as possible. MacKee recommends no surgical procedures, while Klauder, Michelson, Sutton and Wile advise incision of pustules and extraction of comedones. Warren has suggested aspiration of cysts and possibly replacing the contents with penicillin.

Incision of lesions with a cataract knife is adequate in most cases and minimizes trauma and scarring. Comedone extractors are likewise helpful.

D. Physical therapy

1. *X-ray*.—We believe this to be the most efficient single agent in our hands to-day. Its use should be limited to one thoroughly familiar with it. X-ray therapy in full tolerance doses is not 100 per cent effectual and failures are not uncommon. We further advocate its use be withheld except in very severe cases until the age of 15 or 16 has been reached.

2. *Ultra-violet light*.—Unlike x-ray, this form of physical agent has no depressive effect upon over-active oil glands. Its effect is usually temporary and its uses seem to be (1) merely as another peeling agent and one can cause peeling with any speed desired by varying the dosage; and (2) bactericidal, thereby reducing the bacterial flora of the skin.

3. *Cryotherapy*.—It is not widely used but mentioned for thoroughness. A slush is made of carbon dioxide snow, sulphur, and acetone, and applied with a tongue depressor. Marshall advocates it in failures from other treatment, dry skins, and in indurated areas.

E. Hormonal

Liver, thyroid, pituitary and ovarian substances have all been used with great variance of opinion. Nyvell states they are the treatment of choice. MacKee believes they should be used only if indicated by symptoms other than acne. Sutton advocates thyroid in all cases and paratharone in extremely deep-seated types. Wile uses them only for menstrual disorders while Michelson and Miller believe them to be of no value. Osborn agrees in the routine use of thyroid and sees no necessity for a routine basal metabolic rate.

An improvement of 82 per cent is reported with pregnant mares' serum in a group of cases with menstrual disturbances by Birnburg and Rein.

We believe the use of hormones should be restricted to an attempt to regulate menstruation or other glandular disturbances. The absence of such an indicator as the menses in the male leads to their more universal use in that sex.

F. Diet and vitamins

Dietary restrictions are fairly uniform and eliminate or restrict chocolate, iodized salt, fatty, greasy, and highly seasoned sweet and sea foods.

Straumfjord, stressing that acne is due to hyperkeratosis of the pilosebaceous follicle, reports 79 per cent of 100 patients free or nearly so on 100,000 units of vitamin A, daily, for six months or more.

Stokes and Sternberg recommend a high vitamin therapy, stressing vitamin A for follicular keratoderma and vitamin B₁ for constipation.

Pyridoxine has been advocated but any explanation of its rôle is at present speculative. Jolliffe and his

co-workers reported encouraging results using on an average of 25-50 mg. daily initially, the dosage being decreased or increased as indicated clinically.

G. Vaccines, antibiotics, and drugs

Staphylococcic vaccines, toxoids, mixed vaccines and autogenous vaccines have been used and various authors are not in agreement on their benefit. We believe them rational to build up a resistance to secondary invaders but of no value as a primary therapeutic agent.

The use of the various antibiotics and chemotherapeutic agents is attacking the problem from the same point of view, as in the use of vaccine therapy only their effects are even more temporary and secondary than those of vaccine therapy.

H. Cosmetics

The question of their use over a skin affected with acne always presents itself in the handling of female patients. The use of the type of cosmetics that produce a cake-like mask and mechanical follicular plugging, even though temporary, seems contra-indicated. Otherwise, cosmetics should be allowed provided there is no allergic element. Female patients are much more likely to co-operate if cosmetics are not ruled against.

I. Seborrhæa

The treatment of this condition will not be dealt with here. However, because of its frequent occurrence in acne patients, its treatment should be incorporated with treatment of acne.

Relief of Toothache

(From the *Practitioner*, Vol. 163, November 1949, p. 476)

THE following formula for toothache drops is taken from a review in *Pharmacy International*, 1949, 3, 16 (quoted by *Manufacturing Chemist*, August 1949, 20, 398):—

Clove oil	15 ml.
Phenol, liquid	90 ml.
Glycerine	180 ml.
Amaranth solution (1 per cent) sufficient to colour.	

For the temporary relief of toothache it is recommended that a small pledget of cotton wet with this preparation be placed in the socket and then covered with dry cotton.

Gammexane in the Treatment of Head Lice

(From the *Practitioner*, Vol. 163, November 1949, p. 475)

ON the basis of experience in Malaya, a 'simple, rapid and inexpensive' form of treatment of head lice is outlined by J. R. Busvine and J. A. Reid (*Medical Journal of Malaya*, June 1949, 3, 232). The preparation used was 0.2 per cent gamma BHC (gamma isomer of benzene hexachloride) in coconut oil solution, prepared by adding 'one part of "gammexane" concentrate LG 140 [obtainable from Imperial Chemical Industries (India) Ltd.] to 50 parts of coconut oil and stirring. The concentrate LG 140 is an organic solvent containing

10 per cent of a refined grade of gamma BHC which is largely without the rather disagreeable smell of crude samples of BHC'. To prevent accidental ingestion of the medicated oil it is recommended that colouring matter should be added, e.g. 0.1 g. per gallon of the I.C.I. dye known as 'waxoline blue CBS'. The best way of incorporating this dye is to dissolve it first in a few millilitres of chloroform and then add the concentrated solution to the oil. Treatment consisted of applying 10 ml. of the medicated oil to the hair by pipette and distributing it as evenly as possible by rubbing with the hand. Of the 30 children treated in this way, all were free of lice one week later, whereas of 30 children treated with 4 per cent DDT in oil, only 20 were free of lice one week after treatment.

Sodium Propionate in the Treatment of Pruritus Vulvæ

(From the *Practitioner*, Vol. 163, November 1949, p. 475)

BENEFICIAL results are reported by A. M. Davids and A. Kurtin (*American Journal of Obstetrics and Gynecology*, August 1949, 58, 397) from the use of sodium propionate in the treatment of pruritus vulvæ. A 15 per cent sodium propionate ointment, with a vanishing cream base containing a wetting agent, was rubbed into the vulva and perianal skin two or three times daily. In some cases vaginal suppositories of 10 per cent sodium propionate were also used, whilst patients with a vaginal discharge were instructed to use a 5 per cent sodium propionate douche night and morning. Of 15 patients with pruritus vulvæ of one month's to three years' duration, associated with diabetes mellitus, eight obtained complete relief within a week, whilst the remainder required treatment for two to four weeks for 'complete restoration to normal'. Eight patients with mycotic vulvovaginitis were treated by means of the ointment and suppositories, and seven of them obtained complete relief within one to three weeks. Of 22 cases of 'menopausal or atrophic vulvitis', aged fifty to seventy-seven years, only three still complained of irritation after two months of treatment. Most of them began to feel better after a few days, but it was two to eight weeks before the pruritus disappeared completely in this group.

[The following 2 items are reproduced from Surgical Newsletter, Wa-233, dated March 1950, prepared by the American Medical Association]

Early and Delayed Clinical Effects of Vagotomy for Peptic Ulcer

KIPEN AND STEVENS say that between 1st November, 1946, and 1st November, 1947, vagus resection for treatment of peptic ulcer, as recently advocated by Dragstedt, was performed in 42 cases at the Veterans Administration General Hospital at Los Angeles (Sawtelle), California. The patients, all men, varied in age from 20 to 68 years, the average age being 47½ years. One or more of the classic indications for surgical intervention in treatment of peptic ulcer were present in all cases, namely, (1) chronicity with poor response to, or inability to carry out, an adequate medical regimen, (2) hæmorrhage and (3) obstruction.

The duration of symptoms varied from four months to 20 years, the average being 11.2 years. Recurrent or intractable pain was a prominent feature in the majority of these cases. Hæmorrhage, as determined

by a history of hæmatemesis or melena, was present in 16 cases. Obstruction, as determined by retention of barium after six hours during roentgenologic study, was present in eight cases. Twenty-four patients had undergone previous operation for treatment of peptic ulcer. These included 15 patients with perforation treated by simple closure, seven who had undergone previous gastroenterostomy and three who had been subjected to previous partial gastrectomy. Four patients had undergone multiple previous operative procedures; perforation had occurred twice in two, and two others had been subjected to repair of perforation followed at a later date by gastroenterostomy.

In this series, trans-thoracic vagus resection was done in nine cases, abdominal vagotomy without any complementary procedure in 13 cases, vagotomy plus gastroenterostomy in 14 cases and vagotomy plus subtotal gastric resection in six cases.

All cases in this series were included in the early post-operative studies except for one in which operative death occurred which was attributable to mediastinitis following a perforation of the œsophagus in an attempt to isolate the vagi subdiaphragmatically. In the remaining 41 cases there was a rather striking subjective result. Relief of pain was obtained in all cases except two, and both of these patients had overt psychoneurosis, which made subjective evaluation difficult. Twenty-two of the patients had a benign post-operative course, with no immediately recognizable evidence of gastro-intestinal atonia, sphincter achalasia or diarrhœa and no subjective complaints. These patients were able to leave the hospital completely asymptomatic and on an unrestricted diet.

The remaining patients had troublesome symptoms of impaired gastric motility or other immediate untoward complications.

In addition to severe symptoms of gastric atonia as complications in two cases, dysphagia with roentgenologic evidence of œsophageal achalasia occurred in two patients in conjunction with gastric atonia and was troublesome for two and four weeks respectively. Other complications included persistent diarrhœa lasting for two months with spontaneous remission in one case. Intestinal obstruction secondary to previous operative adhesions occurred in another case, necessitating a second laparotomy, after which further convalescence was uneventful. Paralytic ileus complicated still another case but responded well to conservative treatment.

In order to evaluate the procedure in the light of late results, all patients for whom at least three months had elapsed since operation were requested to return to the hospital for examination or to reply to a questionnaire. A total of 25 patients were studied at intervals varying from three to 12 months after operation. Good subjective results were obtained in 85 per cent of the patients in this series, although three of ten patients who underwent vagotomy alone had severe symptoms related to gastric atonia as long as ten months post-operatively. The degree of subjective improvement is more striking and the incidence of complications reduced when complementary gastroenterostomy or gastric resection is done. Although there are too few cases to be conclusive, it seems that best results were obtained in cases in which vagotomy was combined with gastric resection.

Roentgenologic studies revealed that over 75 per cent of patients who underwent vagotomy alone showed decided evidence of gastric retention. With complementary gastroenterostomy, gastric retention was present in over 50 per cent of cases, and with complementary gastric resection this complication was negligible. Roentgenologic studies repeated from three to 12 months post-operatively showed no reduction in the incidence of impaired gastric motility. The operation definitely produced a reduction in gastric acidity which is most noticeable in the response to insulin-induced hypoglycæmia, with a lesser reduction in the

night secretion and relatively little reduction in the response to histamine.

Since the follow-up period in this series of cases does not exceed 12 months, further studies are indicated at subsequent intervals before definite conclusions can be drawn as to the relative merit of vagotomy compared with present standardized surgical methods of treatment for peptic ulcer.

The results of vagotomy as thus far reported in the literature are not as consistently good as those reported for conventional gastric resection by Wangensteen, Walters, Gray, Priestley and Counseller and others. This study further substantiates these reports.

(Kipen, G. S., and Stevens, G. A.: *Archives of Surgery*, 59, 814-824, October 1949. The authors are connected with the Department of Surgery at the United States Veterans Administration General Hospital, Los Angeles and the University of California at Los Angeles.)

Relief of Chronic Hypertension by Excision of Pheochromocytoma

OWENS reports the case of a woman, aged 25. Because of the palpable abdominal tumour with hypertension and a history of attacks which were suggestive of paroxysmal hypertension, it was felt that intra-abdominal exploration was indicated.

The tumour mass on the left side of the abdomen was exposed by retracting the jejunum medially. It was then found that it lay in the retroperitoneal tissues directly over the left lumbar sympathetic chain just medial to the ligament of Treitz and against the left side of the aorta. The mass was approximately 6 cm. in diameter, had a firm capsule and was well demarcated from the surrounding tissues. Numerous nerve fibres were found to run into the posterior aspect of the tumour mass from the left lumbar sympathetic chain. During the manipulation of the tumour the blood pressure and pulse rate had steadily increased, so that just before the last vessels were clamped the blood pressure was 220 systolic and 160 diastolic and the pulse rate 160.

As the main pedicle was clamped the blood pressure fell precipitously to 100 and the pulse rate began to decline.

The patient was discharged from the hospital in excellent condition 12 days post-operatively. The impression gained from the microscopic examination of the tumour was of a characteristic benign pheochromocytoma or chromaffin tumour of sympathetic neural origin arising in the abnormal sympathetic chain, in the vicinity of the Zuckerkandl organ. From the intense chromaffinity, one would expect a high content of epinephrine. The author feels that the extra-adrenal location of the tumour emphasizes the fact that exploration of the adrenals at the time of sympathectomy may not reveal the tumour.

Tests for epinephrine-producing tumours are simple and can be utilized to advantage in the study of the hypertensive patient.

(Owens, Jr., F. M., Chicago, Ill.: *Archives of Surgery*, 59, 896-902, October 1949. The author is connected with the Department of Surgery of the University of Chicago, Chicago, Ill.)

Surgical Treatment of Elephantiasis of the Lower Extremities

(Reproduced from Surgical Newsletter, Wa-230, dated February 1950, prepared by the American Medical Association)

BLOCKER defines elephantiasis as a type of gravitational oedema superimposed upon chronic obstruction

of the lymphatics, aided and abetted by repeated bouts of acute infection.

He feels that too little emphasis has been placed on the rôle which gravity plays in the development of progressive lymphoedema of every variety. Lymphatic obstruction in itself is not so much to be dreaded as the loss of circulatory equilibrium of the affected limb. Tissues which are deprived of their proper blood supply become vulnerable to trauma and infection. The most physiologic approach to the surgical treatment of elephantiasis appears to be the removal of skin and subcutaneous tissue *en masse* down to the uppermost layer of muscles and the periosteum of the tibia; coverage with large thick-split dermatome grafts; and indefinite elastic support for protection against injury and to prevent the inevitable pathologic changes which recurrence of gravitational oedema would entail.

The author presents six cases in which the aforementioned surgical treatment was employed with satisfactory results.

(Blocker, Jr., T. G., Galveston, Tex.: *Plastic and Reconstructive Surgery*, 4, 407-414, September 1949.)

The Clinical Evaluation of Aureomycin

(Reproduced from Medical Newsletter, Wa-227, prepared by the American Medical Association)

BRAINERD and his associates used aureomycin in the treatment of 116 patients with infections due to a variety of bacterial, rickettsial and viral agents.

Adult patients taking aureomycin by mouth generally were given 1 gramme every four to eight hours.

The only significant toxic symptom encountered frequently was nausea and vomiting.

The intravenous route of administration, used in 68 individuals, proved to be an effective method of therapy, both when used to supplement oral medication to produce high serum concentrations of aureomycin, or to replace the oral route in the control of nausea and vomiting.

Aureomycin appeared to exert beneficial effect in acute brucellosis, leptospirosis, Q fever, primary atypical pneumonia, psittacosis, chancre, lymphopathia venereum, generalized peritonitis, and many infections of the urinary tract.

Beneficial effects from aureomycin therapy appeared to be limited or absent in typhoid, Salmonella, Shigella infections, coccidioid pneumonia, infectious mononucleosis, varicella and subacute bacterial endocarditis due to *Streptococcus faecalis*.

(Brainerd, H., San Francisco, Calif., Lennette, E. H., Meiklejohn, G., Bruyn, Jr., H. B., and Clark, W. H.: *Journal of Clinical Investigation*, 28, 992-1005, September 1949. The authors are connected with the Infectious Disease Laboratory of the San Francisco Hospital and the State of California Virus and Rickettsial Disease Laboratory, Berkeley, Calif.)

Epilepsy as a Sequela of Recurrent Malaria

(Reproduced from Medical Newsletter, Wa-247, dated April 1950, prepared by the American Medical Association)

TALBOT and his associates point out that a large number of young men were given medical discharges from the armed services during World War II because of convulsive seizures. Many of these men were stationed in malarial areas at the time of onset of their seizures, and some of them have had recurrent attacks of malaria.

Cerebral pathologic change caused by *Plasmodium falciparum* is a well-known entity. It is only in recent years that the agent of tertian malaria, *Plasmodium vivax*, has been established etiologically with dysfunction of the central nervous system.

Convulsive conditions in patients with malaria are often thought to be idiopathic, because the presence of a malarial infection is considered unrelated or is regarded simply as an agent which lowers the seizure threshold. However, in a significant number of these cases, there is no evidence of previous or of familial epilepsy and none of the other known factors predisposing to seizures. Practically speaking, it is irrelevant whether the malaria is the primary cause of the seizure or a trigger mechanism setting off seizures in a person with a low convulsive threshold. This academic question is of minor importance to the physician who is confronted with a patient disabled with epileptic seizures resulting from malaria.

Cases are presented in which chronic recurrent malaria was the probable causative agent of cerebral damage manifested by convulsive seizures and abnormal electroencephalograms characteristic of epilepsy.

Chronic recurrent malaria must be considered in the differential diagnosis of convulsive seizures, and electroencephalographic examination may be valuable for proper diagnosis.

Pathologic conditions of the central nervous system incident to the severe tropical type of recurrent malarial infection must be vigorously treated. In convulsive conditions, such as those reported, treatment of the malaria is of primary importance. Until this is done, the use of anticonvulsive drugs must play a secondary rôle. Recent therapeutic progress in malaria provides an unprecedented opportunity to halt the process before further damage is done.

(Talbot, D. R., Elerding, A. C., and Westwater, J. O.: *The Journal of the American Medical Association*, 141, 1130-1132, 17th December, 1949. The authors are connected with the Department of Medicine, Wadsworth General Hospital, United States Veterans' Administration Centre, Los Angeles, Calif.)

The Metabolic Fate of the Infused Erythrocyte

(Reproduced from Surgical Newsletter, Wa-250, dated April 1950, prepared by the American Medical Association)

THE nutritional problems of surgical patients have received considerable attention in recent years and since many of these patients receive blood transfusions, Levenson and his collaborators raise the question: 'To what extent do these transfusions contribute to the patients' nutritional requirements?' In particular, should the infused red cell nitrogen, which quantitatively is two to three times greater than the associated plasma nitrogen, be included as intake in day-to-day balance studies?

At present no consistent policy has been adopted in this regard, some investigators including the red cell nitrogen as intake, others not. Where such nitrogen has been included in calculations of daily balance, apparent positive nitrogen balance has been readily attained, and the catabolic phase following injury has apparently been reversed. Other workers, in studies of similar patients, in which, however, the red cell nitrogen was not counted as a source of available nitrogen in the calculation of daily balances, were unable to reverse the negative nitrogen balance following injury. Such conflicting descriptions of results from similar studies indicate a clouded notion of the rôle played in the body metabolism by the infused erythrocyte. To clarify this situation, the present study was undertaken.

Nitrogen balance and erythrocyte survival were studied in two healthy medical students who had been made polycythemic by the infusion of fresh, separated, serologically identifiable red blood cells. Observations were made on body weight, nitrogen balance, circulating plasma protein and erythrocyte mass; erythrocyte survival; serum bilirubin concentration; urobilinogen excretion; and liver function.

Plasma volumes, liver function, and circulating plasma proteins were essentially unchanged throughout the period of the study. Survival time of the infused erythrocytes was not shortened. The infused red cell mass decreased at a normal, expected rate of 0.8 per cent per day. Concomitantly, the mass of the recipient's own erythrocytes declined at a rate of 0.4 to 0.8 per cent per day in direct proportion to the relative amount of the infusions. This progressive fall in the subject's own erythrocyte mass was probably due to erythropoietic depression rather than to abnormally increased destruction. This is suggested by the normal survival of the infused erythrocytes and by urobilinogen excretion consistent with breakdown of the total red cell mass at a normal, not an increased rate. There was a direct linear relationship between the extent of apparent bone marrow depression and the degree of induced polycythemia.

A slow, steady excretion of 0.5 to 1.0 gm. of nitrogen per day (above the control equilibrium value) began shortly after the infusions and continued for one month. The total extra nitrogen excreted was mathematically equivalent to 80 per cent of nitrogen content of the infused erythrocytes. However, this excess nitrogen derived only in small part from the infused red cells. The greater part could be accounted for almost completely by nitrogen diverted from normal erythrocyte synthesis as a result of apparent marrow depression.

The authors feel that it is clear that nitrogen made available to the metabolic pool as a result of erythrocyte infusions is not great, is made available only over a period of weeks, is of unknown biologic efficiency, and quantitatively would contribute little to the overall nutritional requirements. Whether this process is accelerated in patients during catabolic or anabolic conditions is to be studied.

(Levenson, S. M., Birkhill, F. R., Maloney, M. A., and Bell, J. A.: *Annals of Surgery*, 130, 723-746, October 1949. The authors are connected with the U.S. Army Medical Nutrition Laboratory and the Department of Surgery, University of Illinois College of Medicine, Chicago, Ill.)

ERRATUM

In the *Indian Medical Gazette*, June 1950, p. 274, col. 2, under the item 'Chloromycetin in scrub-typhus', para 2, line 1,
for 3 gr. read 3 gm.

Reviews

THE COMMON DISEASES OF THE SKIN: A HANDBOOK FOR THE STUDENTS AND MEDICAL PRACTITIONERS.—By R. Cranston Low, M.D., F.R.C.P.E., F.R.S.E., and G. A. Grant Peterkin, M.B.E., M.B., F.R.C.P. (Edin.). Fourth Edition. 1949. Oliver and Boyd Ltd., Tweeddale Court, Edinburgh; 98, Great Russell Street, London, W.C. Pp. x plus 282 with 148 illustrations of which 9 are in colour. Price, 21s. net

This is an admirable book for undergraduate students and medical practitioners. It is lucid, brief and dogmatic, emphasizing the essential points and

giving clear directions as to diagnosis and treatment. Nowhere has the student been over-burdened with details of special treatments, pathology or theories.

While the book is meant for general-practitioners, also who deal with patients and medicines everyday, the portions on drug eruptions might have been dealt with in a little more detail. More emphasis is also due to pemphigus. Industrial dermatitis has been omitted.

The printing and get-up of the book are good.

D. P.

HAPPY TOIL : FIFTY-FIVE YEARS OF TROPICAL MEDICINE.—By Sir Leonard Rogers, K.C.S.I., C.I.E., F.R.C.P., F.R.C.S., LL.D., F.R.S. 1950. Frederick Muller Ltd., London. Pp. xvi plus 271, Illustrated. Price, 18s. net

THIS book is an autobiography and a textbook on investigation, in the tropics, into all that interferes with health, including snakes. Major-General Sir John W. D. Megaw has written a foreword.

It begins with an account of the education and careers of the boys of the upper middle-class families in England, in the latter half of the last century, nearly a century ago. A reference to the author's father takes one further back to 1824 and sailing ships in which Captain Henry Rogers, R.N., saw a great deal of service.

Sir Leonard's early education was 'at the hands of governesses'. At eight he went as a day boy to Mannamed School, five minutes' walk from home. From ten to twelve he was a boarder at Tavistock Grammar School. Then he was a boarder at another West of England school which remains unnamed: 'It wasted five precious years.' The author sometimes thinks that easy times at different schools enabled him to come 'all the fresher to his medical studies'.

As a day boy at Plymouth College, he worked steadily for the first time and thus began the toil which became happy and happier with each step forward. London matriculation, conjoint diploma, degree and the rest followed, culminating in the I.M.S. in 1893, and the white man's burden in conquering diseases in the tropics. How the burden was carried by Sir Leonard is well known all the world over generally, and in Calcutta particularly, because of his abode in the second city in the empire for 20 years, 1900-1920.

Touches of wit abound: A facetious member of the 'chummers' remarked that 'he did not think it proper for a teetotaler to go to Puri to see snakes at Christmas'..... 'Good God, has Miss North got cholera?' 'No' was the reply. 'She has got him'. (He has gone to the surgical block of the Calcutta Medical College to see his fiancée, before the engagement was announced, and his car was seen by a resident medical officer.)

Sir Leonard first brought hope to the leper when he systematized the treatment with concentrated and refined drugs, thus telescoping into months of hopeful co-operation previous years of indifferent medication given and taken more to satisfy a routine than attain any result within a reasonable period. In one year he cured a comrade in the I.M.S., who remained free from the disease for ten years, up to his death in a motor car accident.

The Calcutta School of Tropical Medicine, which houses Sir Leonard's bust (facing p. 176 in the book), is one of the results of the happy toil lasting ten years, from 1910 to February 1920, when Sir Leonard handed over the scheme of organization to Major R. Knowles, on leaving India.

No worker on tropical diseases can do without a reference to Sir Leonard's contributions to the

knowledge concerning them. Essential features of all such contributions will be found in this book complete with charts, graphs, diagrams, maps and photographs. The fact that medication has changed does not alter the modes of approach to the problems. Some of them have not progressed much beyond where he left them.

Sir Leonard left India in 1920 and 'thus ended twenty years of strenuous research work in Calcutta with unique opportunity at a time when tropical medicine furnished an almost virgin field for investigation..... I was fortunate in being able..... to make the most of opportunities such as can never return'.

And then began the happy toil in England, work in the India Office and in the B.E.L.R.A.

Sir Leonard is toiling happily at 81. For his constitution toil appears to be necessary for his happiness: Hence the decision to walk through the jungle in Assam, after 4-10 p.m., for 4 hours, with a leopard behind for a part of the journey, in 1896-1897. To this disregard for safety and comfort he also added, so records Sir John Megaw, lack of attention to dress and personal appearance, before he married. To Lady Rogers then, evidently, the medical world is indebted for the present fitness of Sir Leonard. The book is also dedicated to Lady Rogers.

The book is remarkably complete in details because Sir Leonard kept a brief shorthand diary of his doings.

A remarkable book by a remarkable man with a foreword by another remarkable man.

S. D. S. G.

HANDBOOK OF OBSTETRICS AND DIAGNOSTIC GYNÆCOLOGY.—By Leo Doyle, M.D., M.S. First Edition. 1950. University Medical Publishers, California. Pp. 240. With illustration by Ralph Sweet

THIS little handbook will be well appreciated by advanced students preparing for a viva voce examination. All important topics have been dealt with in a masterly way. The style is easy and concise. Essentials have been given their proper place, for the sake of brevity, details have not been discarded.

Many illustrations have been included. Most of them are self-explanatory and descriptive of the matter in the text—e.g. the diagram in chapter 12 describing the sites of ectopic pregnancies and in chapter 15 describing the various types of placenta previa. The diagram illustrating the Rh factor in erythroblastosis is well appreciated.

The printing is good but may be difficult to appreciate by persons who have to study in insufficient light.

We recommend this book to the students and practitioners.

M. N. S.

APPLIED MEDICINE.—By G. E. Beaumont, M.A., D.M., F.R.C.P., D.P.H. 1950. J. and A. Churchill Ltd., London, 104, Gloucester Place, London, W.1. Pp. ix plus 540, with 74 illustrations. Price, 30s. net

THIS book by a well-known teacher presents problems in individual cases and their solutions.

In part I are described 33 cases of as many diseases, including many more diseases, of course, in the differential diagnosis.

In part II are given short notes on 17 cases. Some of these cases emphasize recent advances in medicine particularly well. Such is the first country case of the author, a case of Grave's disease, with a high temperature and uncontrollable restlessness (p. 231). The

patient died in accordance with the prognosis given in **OSTLER'S MEDICINE**: 'An important complication is acute mania, in which the patient may die in a few days.' This occurred about fifteen years ago. No effective treatment was then known. The milk of thyroidectomized goats was seriously recommended. Later became available Lugol's iodine solution and later still thiouracil. To-day a similar case will live.

Part III is a magic carpet and takes the reader to the author's ward in London to hear all that can be said relevantly (or even irrelevantly) on 24 cases. Perhaps the best case in differential diagnosis is one of P.U.O. which turns out to be one of Typhoid Fever diagnosed by the Widal reaction.

June 14th

Typhoid H positive in 1 in 1280.

" O negative.

Para A "

" B "

June 20th

Typhoid H positive in 1 in 640.

" O " " 1 in 640.

Para A " " 1 in 40.

" B " " 1 in 80.

The discussion is specially useful in Indian practice in which 'fever' predominates, particularly in military hospitals where patients stay as long as required and co-operate as a matter of duty.

The case of Hibernating Gland provides a rare condition and so do cases of Diffuse Lupus Erythematoses.

Part IV provides over 6 pages of 'Idle thoughts' which really are crystallized wisdom of a mature physician: 'Rest and be saved' in tuberculosis; 'Little worries produce asthma and big ones remove it by adrenalin output' in neurosis.

An index provides a quick means of obtaining the author's view on any item falling under recent advances and also some old items so beloved of old fashioned examiners, e.g. cracked-pot sound, not yet heard by the author (p. 251).

The paper and printing are good. The binding could be better. Only two printing faults have attracted attention (pp. v, the first line in the book and 75, the legend to a very important photomicrograph). The price perhaps could be lower.

An excellent publication.

S. D. S. G.

CURRENT THERAPY, 1950. LATEST APPROVED METHODS OF TREATMENT FOR THE PRACTISING PHYSICIAN.—By Howard F. Cohn, M.D., and Twelve Consulting Editors. W. B. Saunders Company, Philadelphia and London. Pp. xxxii plus 736. Price, 60s.

THE book representing the work of more than 250 contributors gives the latest approved methods of treatment for the practising physicians. In this edition many additions and alterations have been made to bring the book up to date, and no pains seem to have been spared to make it practical and useful to practitioners. We, however, consider that the congenital anomalies described on pages 316-321 are out of place in a book of this kind. The two methods of treatment of gonorrhoea might have been given together in the same place instead of separating them out under two different sections (pp. 355 and 402). The book is well produced and it is easy to locate the desired information.

R. N. C.

A TWENTIETH CENTURY PHYSICIAN: BEING THE REMINISCENCES OF SIR ARTHUR HURST, D.M., F.R.C.P. With a Foreword by Professor John A. Rylo, M.D., F.R.C.P. Published by Edward Arnold and Co., London. Pp. viii plus 200. With Illustrations. Price, 15s. net

This book is the life of the late Sir Arthur Hurst, the well-known London physician, written by himself and edited by Professor Rylo. In addition to describing the emergence of the new physician of the century, in England, it gives an insight into the economic cultural, social and professional developments in Europe during the latter part of the last and nearly the half of the present century.

Born in Caul, on 23rd July, 1879, at Bedford, the writer remembers as the first event in his memory eruption of the Karaka-ton, Eastern Java and Sumatra in 1883 at the age of four.

Back to England; Bedford, Manchester and Oxford (1897-1901), the writer patronized a small but effective repair shop in Longwall. The enterprising owner only 2 years older than the patron later emerged as Viscount Nuffield.

At Guy's, 1901-1905, the writer learnt his profession under masters of medicine and surgery who wore elaborate tiepins with morning dress. House appointment, M.R.C.P. Radcliffe Travelling Fellowship followed.

Visiting Germany in 1905, he once stayed at Munich in a pension which provided a bed-sitting room and three good meals for 5 marks a day. Two other boarders were a retired actor and his wife both in their eighties. They admired translations of Oscar Wilde's works and believed them and 'Oskar' to be German. They had to be convinced that Wilde was an Irishman, educated at Oxford at writer's Own College. To the pension used to come a merchant from Berlin once a month on business and for a complete bath on the morning after his arrival. He had no bath in his residence in Berlin. The writer forgot his priority for the bath on the morning in question and the merchant banged at the bathroom door and uttered a torrent of abuse at the Englander who had stolen his bath. He had his compensation at dinner when he was able to expose Frau General Bangel: The Herr General was a General Director, not an Army General at all.

From Germany the writer went via Italy to Spain. At one university town he made a round with a professor of medicine and his student. They wore their hats and smoked at the bedside of the patients, spitting from time to time on the stone floor. He also visited hospitals for lepers outside Seville, Granada. The patients in various stages of the disease appeared quite happy and included several convalescent patients from the neighbouring smallpox hospital. A beggar had also taken his residence there from sheer laziness. Back to Strasbourg, in Germany, went the writer. Strangely, he remembers nothing about his residence in Strasbourg.

The writer visited America next. But the reviewer must bring him back to London (to the post of a junior physician, at Guy's, after a few intermediate stops, to Active Service in the World War I, to the post of a senior physician in the same hospital, to fame, to opulence and to Honour) to find room for two astounding items so boldly described in the book.

1. AN ADVENTURE IN CARDIOLOGY

One day, in May 1908, the writer with his home physician came to the bedside of a red-haired young woman with rheumatic heart disease. The veins in her neck were beating rapidly although her heart sounds and pulse were normal. They thought of James Mackenzie's polygraph which was obtained and used. The beautiful tracings showed that pulse in the neck vein was 234 while that in radial artery was only 70. The case was shown to James Mackenzie. A

manuscript for a paper was prepared and also shown to him. Later, the paper was published in the *Quarterly Journal of Medicine*. Mackenzie had read the proof and had approved of the title 'The Maximum Rate of Human Heart'. A few months later, when a reprint was sent to Mackenzie, the latter acknowledged it on a post card: 'Thank you for the reprint with excellent tracings. But why describe a typical case of nodal rhythm under such an idiotic title?' As a matter of fact he had formed the conception of 'nodal rhythm' after he had returned the proofs. He had a bad memory for time as he had told the writer more than once. Two years later on meeting the writer casually in Harley Street, he stopped the latter and wanted to know what had become of the latter's case of auricular fibrillation. On the writer reminding him of the previous diagnosis of nodal rhythm, the latter said 'no, no, it was a case of auricular fibrillation'. During the intervening two years electrocardiogram had been used and it had diagnosed such an abnormality as auricular fibrillation. In 1919 Professor W. T. Ritchie of Edinburgh sent the writer a reprint of a paper he had just written on auricular flutter. The account agreed with the account recorded for the red-haired woman. The case really was one of auricular flutter.

2. MEDICAL EDUCATION IN GERMANY AND ELSEWHERE IN EUROPE

The writer found on revisiting Germany in 1931 that medical education had not changed much since his last visit in 1905-1906. Students attended an enormous number of lectures and gained a good deal of theoretical knowledge, but they had very little contact with patients. There were no appointments for them corresponding to the ward-clerks and dressers of British medical schools. The same defect existed in Switzerland, Holland and Scandinavia. The average British general practitioner was far superior to his Continental colleague.

These are samples, not random, from the book. The reader will find many more items of absorbing interest in medicine, surgery, homœopathy and other means of dealing with sick people. He will also find scenes from domestic happiness, painting, poetry and other human values.

Sir Arthur died suddenly on 17th August, 1944, and was cremated in accordance with instructions in verse quoted from John Galsworthy (once his patient).

Scatter my ashes !
Let them be free to the air,
Soaked in the sunlight and rain,
Scatter with never a care
Whether you find them again.
Hereby I make it a trust :
In no grave be confined,
Mingle my dust with the dust,
Give me in fee to the wind.
Scatter my ashes !

Book Notice

WE have received a copy of Therapeutic Notes from the Bengal Immunity Research Institute. It includes a long list of various preparations, injectables, vaccines, sera, B.I. specialities, etc., with their indications,

method of administration and dosage. There is also a list of diseases against which are mentioned the various preparations that may be used.

Abstracts from Reports

REPORT OF THE SCIENTIFIC ADVISORY BOARD, IRFA, FOR THE YEAR 1949

Of the many researches carried out during the year, the following may be mentioned, being of more general interest.

Cholera.—An investigation has been started under K. V. Veukaram (King Institute, Guindy) on the possibility of sub-clinical cases of cholera constituting a link between successive outbreaks of cholera in the Cauvery Delta. The selected villages have been surveyed and a systematic examination of faecal and water specimens has commenced. S. C. Ghosal (School of Tropical Medicine, Calcutta) is carrying out certain bacteriological tests in the diagnosis of cholera. K. V. Krishnan (All-India Institute of Hygiene and Public Health) carried out the study of agglutinin response to anti-cholera inoculation in normals, vaccinated persons and recommended cholera cases and obtained interesting results.

Malaria.—Studies on different insecticidal formulations were continued under Lieut.-Colonel Jaswant Singh (Malaria Institute of India) both in the laboratory and the field in Delhi and Coonoor. R. N. Chaudhuri (School of Tropical Medicine, Calcutta) has been working on the chemotherapy and chemoprophylaxis of malaria. In a study on comparative efficacies of paludrine, chloroquine and camoquin he has found that the action of chloroquine is quick, paludrine slow and camoquin intermediate. A strain of *falciparum* parasite resistant to paludrine has been studied. His work in the rural areas shows that chemoprophylaxis can bring about a striking decline in malaria incidence; the work is still continuing. K. Ganapathi (Haffkine Institute, Bombay) has synthesized a large number of anti-malarial compounds, but none proved effective so far. Chloroquine prepared in the Institute showed activity.

Nutrition.—A number of studies on vitamins, protein metabolism and nutritional factors in liver disease is in progress under V. N. Patwardhan (Nutrition Research Laboratory, Coonoor). A variety of nutritional disorders was treated at the clinic of the Institute. Cases of phrynodema responded fairly well to gingelly oil, the condition being often associated with very low fat content of the diet. There were 18 cases of 'malignant nutrition'—all children 15 to 42 months old, having steatorrhœa and œdema with dry skin with or without braun desquamation and in some cases other dermal lesions, angular stomatitis or xerosis with Bitot spots. Blood showed aemia dimorphic or hypochromic type. The disease is probably identical with Kwashiorkor or South and East Africa. Circumcorneal pigmentation was a common condition seen among children in the Nilgiris during nutrition surveys; its cause is unknown. R. G. Chitra (Seth G. S. Medical College, Bombay) found no trace of thiamine and riboflavin in samples of rice and wheat stored under ordinary conditions since 1944, showing that such storage is not conducive to the retention of these vitamins. A feeding experiment carried out in school children by B. N. Banerjee and S. S. De (Indian Institute of Science, Bangalore) showed that soya-bean curd has a nutritive value like that of separated milk curd when given as a supplement. An inquiry into malnutrition among poor classes by (Mrs) S.

Chandhuri and K. Mitra (Lady Hardinge Medical College Hospital, New Delhi) revealed very low caloric values of their diet (1,000 to 1,600 per calories) with low plasma proteins in most cases and low blood volume in anemia cases. Animal proteins or protein hydrolysate caused definite improvement. Iron, liver extract or folic acid alone was not so effective as when proteins were added.

Leprosy.—Dharmendra (School of Tropical Medicine, Calcutta) was concerned mainly with the investigation on the use of sulphatrene by intramuscular injections. This method is very economical and possibly more effective. Para-amino salicylic acid was tried in 2 cases of leprosy with some clinical improvement. R. G. Cochrane (Lady Willington Leprosy Sanatorium, Chingleput) has continued work on histopathological changes in leprosy. A detailed report on his studies of sulphone therapy is in preparation.

Plague.—In experimental plague infection in mice General Sokhey (Haffkine Institute, Bombay) found aureomycin as effective as streptomycin and chloromycetin less effective than either of these drugs. Though cyanogas fumigation is still the sheet-anchor in the control of plague, D.D.T. (10 per cent) insufflated into rat holes has been found in the Nilgiris district as a very effective pulicide, keeping the flea index very low (Director of Public Health, Madras). R. B. Lal and S. C. Seal (All-India Institute of Hygiene and Public Health, Calcutta) are making a study of the epidemiological features of plague in Calcutta.

Clinical research.—The rôle of nutritional factors in hepatic cirrhosis was studied by M. V. Radhakrishna Rao (Haffkine Institute, Bombay) and interesting results were obtained. Clinical and biochemical investigations on infantile hepatic cirrhosis were continued under V. Subrahmanyam and V. R. Naidu (Central Food Technological Research Institute and S. K. Hospital, Mysore). Results obtained so far have shown that pepsin-proteolyzed extract of the liver and spleen supplemented by choline chloride is much superior in therapeutic effect to choline chloride alone. To help digestion, dietetic management is necessary and fat should be eliminated or minimized in the diet. Liver biopsy should be carried out to get a picture of the histological changes at different stages of the disease and the findings should be correlated with liver function tests. K. V. Krishnan (All-India Institute of Hygiene and Public Health) made a study of the clinical, epidemiological and transmission aspects of typhus in Bengal. In the treatment of 4 cases, aureomycin brought the temperature to normal within 24 hours and there was complete recovery in 72 hours. Lient-Colonel S. D. S. Greval (School of Tropical Medicine, Calcutta) tested 75 subjects for iso-immunization, antibody was found only in five. B. Mukerji (Central Drugs Laboratory, Calcutta) investigated chromatophoretic hormone of the pituitary gland. C. R. Das Gupta (School of Tropical Medicine, Calcutta) carried out hæmatological studies in pregnant women, plague, leukaemia, etc.

Maternity and child welfare.—An inquiry by Muktha Sen (All-India Institute of Hygiene and Public Health) in the Singur Health Centre showed that the sickness rate among children 1 to 5 years old was highest in age group 1 to 2 years, gradually decreasing in successive years. Common causes of illness were cold, diarrhoea, boils and fever. Among children of 1 to 2 years, two had cut no teeth yet and four had only two teeth. As to the motor control, two could only sit and four could only crawl. Another inquiry by the same author with K. K. Mathur was into the vital losses of pregnancy and infancy among women in the same health centre. The inquiry is in progress, but so far the records show that the still-birth rate is roughly 5 and the abortion rate 2 per 100 live-births. The latter figure is thought to be an under estimate. In spite of a maternity home and hospital in the locality, most women prefer to be delivered in their

own homes.* The percentage of abnormals are not very high, of 1,483 live-births there were as many as 174 prematures among which there was high mortality.

Pharmacology.—This relates mostly to indigenous drugs. J. C. Gupta has found *Damia extensa* Linn. to have properties like ergot and pituitrin and its usefulness in conditions like menorrhagia, metrorrhagia and subinvolution of uterus. Colonel R. N. Chopra reports on a fern, *Dryopteris blanfordii*, and says it can be used as an anthelmintic against tapeworms. He also tested some commonly used drugs in Ayurvedic and Unani medicine and found them adulterated.

Correspondence

GENERALIZED CYSTICERCOSIS CELLULOSA

SIR,—With reference to my article on 'Generalized cysticercosis cellulosa' which appeared in March 1950 in your journal, I have to bring to your kind notice that I missed to take a note of 3 cases of cysticercosis in man reported by Dr. Menon and Dr. G. D. Velath from Madras reported in *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXXIII, No. 5, pp. 537-544 (issued 20th March), 1950.

Yours faithfully,
C. J. DAVE.

110, MEADOWS STREET,
FORT, BOMBAY 1.

PALUDRINE POISONING

SIR,—Noted the contents of 'A case of accidental paludrine poisoning' in your July 1950 issue with interest.

This case illustrates the marked gastro-intestinal and urinary symptoms produced after ingestion of very heavy doses (1.8 gm. daily for two consecutive days) of paludrine, which are not required for therapeutic uses.

Here I like to bring to the notice of your readers that I have noticed symptoms of marked gastro-intestinal irritation produced by very small doses of paludrine. I have noticed this in two adult patients who tried to take 2 tablets of (0.1 gm. each) paludrine for prophylactic use once a week. Both of them narrated identical experience.

For the first time they took it; within half an hour of their taking it, they experienced marked nausea and giddiness accompanied with abdominal discomfort and a feeling of prostration, and this forced them to take a recumbent position in their beds. Soon it was followed by vomiting and it was after that their symptoms started declining and it took several hours for them to feel and become normal.

*In this connection see also a communication entitled 'A study on the health habits of a rural community in West Bengal in the matter of medical relief with special reference to the utilization of free medical service' by R. B. Lal and S. C. Seal, and another communication entitled 'Unwanted medical relief' by S. D. S. Greval in the *Indian Medical Gazette*, 83, pp. 521 and 320. Medical relief as given is unwanted mostly.—Editor, I.M.G.

Every time when they attempted to take the drug these symptoms reappeared.

When the complaint was brought to my notice I advised them not to take the paludrine tablets with their morning cups of tea as they used to do so far, but after meals and preferably when going to bed.

And thus they could successfully take paludrine tablets for prophylactic purposes.

Yours faithfully,
SURENDRA NATH GUPTA.

CIVIL HOSPITAL,
LALITPUR.

ADVERTISEMENTS IN MEDICAL JOURNALS

SIR,—I am tired of advertisements. To pick up genuine things from heaps of rubbish has become very difficult. I find advertisements of new medicine from new mushroom firms daily. Naturally all cannot be relied upon. So be pleased to inform the public whether the advertisements regarding medicines that are found in the *Indian Medical Gazette* or in other journals are genuine, reliable and can be safely prescribed, and whether they are given permission by Government or any other authentic body to advertise as they do.

Yours faithfully,
I. B. MUKHERJEE,
Medical Officer, Nawpara.

P. O. HARADHAN,
NADIA.

[The practice in the office of this journal is that every advertisement is scrutinized with the aid of specialists. Many advertisements are rejected or modified.—EDITOR, I.M.G.]

Any Questions

OPHTHALMOLOGICAL JOURNALS

SIR,—As I am interested in subscribing for the ophthalmological journals, I will be grateful if you will give me a few addresses of publishers of ophthalmological journals in India as well as abroad.

Yours faithfully,
R. G. LAVI, L.M.P., L.O.

ONGAUM.

[The following addresses may be useful :—

1. Indian Journal of Ophthalmology,
502, Narayan Peth, Poona City, India.
2. American Journal of Ophthalmology,
Ophthalmic Publishing Co.,
664 N., Michigan Avenue, Chicago 11.
3. Archives d'Ophthalmologie,
Masson (), Saint-Germain,
Paris 6.
4. Archives of Ophthalmology,
American Medical Association,
535, North Dearborn Street, Chicago 10.

5. The British Journal of Ophthalmology,
George E. Pulman and Sons Ltd.,
24, Thayer Street, Marylebone, London,
W.1.

6. Bulletin of Practical Ophthalmology,
Green's Eye Hospital,
Bush and Octavia Street, San Francisco.

—EDITOR, I.M.G.]

TREATMENT OF THREAD-WORMS

SIR,—In the *Indian Medical Gazette* issue, dated July 1950, there is a question by Miss K. S. Soman (under Any Questions) about the treatment of 'Thread-worms'.

There is a specific remedy 'Diphenan' of B.D.H. which has the outstanding advantages of being highly toxic to thread-worms, readily tolerated by even the youngest patients. These are tablets, and could be beneficially used.

Yours faithfully,
K. N. DATHATHRI.

SHIMOGA.

Publishers' Notice

SCIENTIFIC Articles and Notes of interest to the profession in India are solicited. Contributors of Original Articles are entitled to receive 25 reprints gratis; additional reprints can be obtained on payment. No reprints will be supplied unless contributors ask for them at the time of submitting their manuscripts.

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CONTENTS

	Page		Page
ORIGINAL ARTICLES		FIRST DEPUTY DIRECTOR-GENERAL OF W.H.O. APPOINTED .. 461	
Acute Gastro-enteritis due to <i>T. vincenti</i> and <i>B. fusiformis</i> . By L. M. Sanghvi, M.R.C.P. (Lond.), D.T.M. & H. (Eng.), and Captain P. Subrahmanyam, B.A., B.Sc., M.B., B.S. .. 437	437	DELHI TRAINING CENTRE FOR CHILDREN'S DOCTORS AND NURSES PLANNED .. 461	461
Two Instances of Proved Rabies in the Tiger. By S. R. Pandit .. 441	441	MALARIA RATE REDUCED IN AREA OF PAKISTAN SPRAYED IN PROJECT OF W.H.O. AND U.N. CHILDREN'S FUND .. 461	461
An Outbreak of Plague in an Epidemic Form treated with Streptomycin and Sulfadiazine. By P. K. Ghosh, M.B. 441	441	POLAND ANNOUNCES DECISION TO WITHDRAW FROM WORLD HEALTH ORGANIZATION 462	462
Insulin Resistance in Diabetes Patients. By J. P. Bose, M.B., F.C.S. (Lond.), F.N.I. .. 445	445	W.H.O. EXPERT GROUP DEFINES PRINCIPLES OF HEALTH CARE NEEDED BY SCHOOL-AGE CHILDREN .. 462	462
Hydrophobia in India. By M. L. Ahuja, M.D., D.P.H., Lieutenant-Colonel, and A. G. Brooks, D.T.M. .. 449	449	W.H.O.-UNICEF EXPERTS TO AID IN YAWS-CONTROL CAMPAIGN IN THAILAND 463	463
Serological Technique : Immunotherapy (contd.). Immunization against Rabies. By S. D. S. Greval, Lieutenant-Colonel, I.M.S. (ret'd.) .. 453	453	W.H.O. TO SEND HEALTH OFFICERS TO KOREA TO AID IN RELIEF PROGRAMMES FOR CIVILIANS .. 463	463
A MIRROR OF HOSPITAL PRACTICE		CARIBBEAN RABIES CONFERENCE RECOMMENDS CO-ORDINATION OF RABIES CONTROL IN AREA .. 463	463
Vaginal Cyst. By N. C. Sen, M.B. (Cal.), D.G.O. (Dub.), F.R.C.S. (Edin.) 455	455	AUSTRALIA LOOKS FOR VEGETABLE DRUGS 465	465
ERRATUM .. 456		AUSTRALIA'S BLOOD DONATION SERVICE. By Leo Kelly .. 465	465
EDITORIAL		THE QUEEN VISITS NOTTINGHAMSHIRE .. 466	466
Rabies .. 457	457	ELECTRICALLY CONTROLLED PAGE-TURNER 467	467
MEDICAL NEWS		British Journal of Tuberculosis and Diseases of the Chest .. 467	467
PRESS NOTE .. 460	460	INDIAN PHARMACEUTICAL CONGRESS .. 467	467
MAN'S EXPECTATION OF LIFE 'CONSIDERABLY INCREASED' .. 460	460	FACILITIES FOR POST-GRADUATE MEDICAL STUDIES .. 468	468
NEW SUPER X-RAY MACHINES FOR CANCER TREATMENT .. 460	460	NUFFIELD FOUNDATION TRAVELLING FELLOWSHIPS AWARDS TO INDIAN GRADUATES ... 468	468
W.H.O. ANTI-MALARIA PROJECT IN REMOTE AREA OF NORTH AFGHANISTAN .. 460	460	PUBLIC HEALTH SECTION	
		A 'New Latrine' Suitable for Rural Communities, Camps and Isolated Bungalows. By R. B. Lal, F.N.I. .. 469	

(Continued on page 436)

CONTENTS—(Continued from page 435)

	Page		Page
FIFTY YEARS AGO			
MOSQUITOES AND MALARIA IN CALCUTTA (<i>Indian Medical Gazette</i> , October 1900, Vol. 35, p. 400)	473	AUREOMYCIN IN THE TREATMENT OF INFECTIOUS DISEASES. By H. M. Rose and other (<i>American Journal of Medicine</i> , Vol. 7, October 1949, p. 532, as abstracted in the <i>International Medical Digest</i> , Vol. 56, January 1950, p. 8)	476
CURRENT TOPICS, ETC.			
THE FOOD HABITS OF <i>Entamoeba histo-</i> <i>lytica</i> . By C. A. Hoare (<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i> , Vol. 43, July 1949, p. 7)	474	CONTINUOUS ANTIBIOTIC THERAPY: A NEW METHOD FOR HOME AND OFFICE. By N. Steinberg (<i>Journal of the American Medical Association</i> , Vol. 142, 21st January, 1950, p. 173)	478
STUDIES ON THE EFFECT OF THE ADMINIS- TRATION OF PITUITARY ADRENOCORTICO- TROPIC HORMONE (ACTH) TO A CASE OF LOEFFLER'S SYNDROME AND A CASE OF TROPICAL EOSINOPHILIA. By P. Herbert et al. (<i>Journal of Allergy</i> , Vol. 21, January 1950, p. 12)	474	CLINICAL AND BIOCHEMICAL STUDIES IN CHOLERA AND THE RATIONALE OF TREAT- MENT. By M. H. Ghanem and other (<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i> , Vol. 43, July 1949, p. 81)	478
RELAPSE IN TYPHOID FEVER AFTER TREAT- MENT WITH CHLORAMPHENICOL. By J. N. Briggs (<i>Lancet</i> , i, 21st January, 1950, p. 115)	475	CONTINUOUS INTRAGASTRIC DRIP IN THE TREATMENT OF PEPTIC ULCER. By H. W. Garlick (<i>Medical Journal of Australia</i> , Vol. II, 24th September, 1949, p. 453) ..	481
THE EFFECT OF RIGID SODIUM RESTRICTION IN PATIENTS WITH CIRRHOSIS OF THE LIVER AND ASCITES. By W. J. Eisen- menger et al. (<i>Journal of Laboratory and Clinical Medicine</i> , Vol. 34, August 1949, p. 1029)	475	REVIEWS	
A NEW METHOD OF DIAGNOSIS OF KALA- AZAR. By N. G. S. Raghavan (<i>Indian Journal of Malariology</i> , Vol. 3, June/September 1949, p. 199) ..	475	NUTRITION AND DIET IN HEALTH AND DISEASE. By James S. McLester, M.D. <i>Fifth Edition</i> . 1949	481
A CASE OF CUTANEOUS AMOEBIASIS. By W. Armstrong (<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i> , Vol. 43, July 1949, p. 79) ..	475	HANDBOOK OF COMMUNICABLE DISEASES FOR THE USE OF MEDICAL OFFICERS OF SCHOOLS: FORMERLY A CODE OF RULES. <i>Eleventh Edition</i> . 1948	481
KALA-AZAR: RELAPSE FOLLOWING SPLENEC- TOMY. By T. C. Morton (<i>Transactions of the Royal Society of Tropical Medicine and Hygiene</i> , Vol. 43, July 1949, p. 8)	475	A TEXTBOOK OF BACTERIOLOGY. By N. G. Pandalai, M.D., D.T.M., F.R.C.P. (<i>Edin.</i>). 1948	482
THE TREATMENT OF FALCIPARUM MALARIA WITH INTRAMUSCULAR CHLOROQUINE. By C. G. Spicknall et al. (<i>American Journal of Medical Sciences</i> , Vol. 218, October 1949, p. 374, as abstracted in the <i>Inter- national Medical Digest</i> , Vol. 56, January 1950, p. 7)	476	DISORDERS OF SEX AND REPRODUCTION: ÆTIOLOGY, DIAGNOSIS AND TREATMENT. By A. P. Pillay, O.B.E., M.B., B.S. 1948	482
		BOOKS RECEIVED .. 482	
		CORRESPONDENCE	
		PARENTERAL USE OF VITAMINS ..	482
		CLINICAL HYDROPHOBIA WITHOUT CONTACT WITH RABIES TRANSMITTING ANIMAL ..	483
		SERVICE NOTES .. 483	

Original Articles

ACUTE GASTRO-ENTERITIS DUE TO *T. VINCENTI* AND *B. FUSIFORMIS*

By L. M. SANGHVI, M.R.C.P. (Lond.),
D.T.M. & H. (Eng.)

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and

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IN 1948 and 1949, between the months of July and October, we had in Bikaner two outbreaks of severe gastro-enteritis. The cases in these outbreaks presented a typical clinical picture of cholera, with severe vomiting and profuse watery painless diarrhoea, and attendant dehydration and circulatory collapse.

In the first outbreak of 1948, attempts to isolate *Vibrio cholera* or other intestinal pathogens proved futile. Before any further investigation could be carried out, the outbreak subsided. It was however noticed that almost all the stool specimens showed the presence of *Treponema vincenti* and *Bacillus fusiformis*. No particular importance was attached to this finding at the time, as these organisms sometimes can occur in normal stools. These cases were treated with sulpha group of drugs in addition to the usual line of treatment for cholera.

In July 1949, a similar outbreak appeared again. This time also all attempts to isolate *Vibrio cholera* or any other intestinal pathogens were unsuccessful. We were again struck by the constant presence of *T. vincenti* and *B. fusiformis* in the stools as well as in the vomits of all the patients. This led us to think of the possibility of these organisms playing an aetiological rôle in these cases. Owing to technical difficulties the organisms could not be isolated in pure culture.

Since arsenical preparations have a specific effect on spirochætal infections, we made a therapeutic trial with them. In spite of the doubts expressed by Jewsbury (1943) as to the efficacy of arsenicals in Vincent's angina, the results in our cases were miraculous and in most cases a single injection of an arsenical was all that was necessary to effect complete cure in a short time.

Some of the typical cases are reported below :—

Case 1

A Hindu male, 16 years. Admitted 2nd September, 1949, 2 p.m. History of ten vomits and 12 watery stools during the previous 16 hours.

Condition on admission.—Collapsed, dehydrated, pulse imperceptible, sunken eyes, pinched face, skin dry and inelastic, muscular cramps. Temperature subnormal; blood pressure, systolic below 50 mm. Hg.

Stool examination.—Whitish, watery (rice-water) with a few white flakes.

Microscopic.—A few pus cells and epithelial cells. No ova or cysts, no *E. histolytica*, no vibrio. Stained smear showed *T. vincenti* and *B. fusiformis* in large numbers.

Culture.—No pathogens grown.

Routine urine and blood examination.—N.A.D.

On admission, treatment started with sulphaguanidine 4 tablets 2 hourly; 600 cc. hypertonic saline and 2,700 cc. normal saline intravenously with 2 ampoules of coramine; camphor in oil 3 cc. 6 hourly; per corten 1 ampoule 6 hourly; mist. chlorotone 4 hourly.

Progress.—On 3rd September, 1949, the patient had 17 motions and 4 vomits. General condition same. 2,300 cc. normal saline intravenously repeated.

4th September, 1949.—Had 13 motions and 4 vomits. 1,000 cc. normal saline intravenously repeated.

6th September, 1949.—Continuous leaking from rectum; 3 vomits; general condition bad. Stool: *T. vincenti* and *B. fusiformis* still present. Sulphaguanidine stopped. Mapharside 40 mg. intravenously given; 800 cc. saline intravenously repeated.

7th September, 1949.—Condition much better; only one normal stool and no vomit after mapharside injection. Stool: no *T. vincenti* or *B. fusiformis* seen.

12th September, 1949.—Discharged cured.

Case 2

A child, ten months. Admitted 2nd September, 1949. History of continuous vomiting and diarrhoea for 24 hours. Had two attacks of generalized convulsions.

Condition on admission.—Collapsed, dehydrated, pulse rapid and feeble, temperature 102°F., restless. Lungs: signs of broncho-pneumonia. Vomit and stool: same as in case 1; only *T. vincenti* and *B. fusiformis* seen. No pathogens on culture. Blood: mild leucocytosis. Total W.B.C. 12,000, polymorphs 60 per cent. No malarial parasite.

On admission, treatment started with penicillin 15,000 units intramuscularly 3 hourly, 500 cc. saline subcutaneously, sulphaguanidine 1 tablet 2 hourly, bromides.

Progress.—On 4th September, 1949, the temperature was normal. Lung signs cleared. No improvement in diarrhoea and dehydration; saline 250 cc. subcutaneously given.

6th September, 1949.—Condition same. Temperature normal. Saline 500 cc. subcutaneously repeated. Penicillin stopped.

9th September, 1949.—Condition remained the same till 9th. Stool examination revealed large numbers of *T. vincenti* and *B. fusiformis*. Sulphaguanidine stopped; acetylarsan 1 cc. intramuscularly given. Six motions.

10th September, 1949.—Condition better. No vomit. One motion. *T. vincenti* and *B. fusiformis* not seen in the stool.

11th September, 1949.—Condition improved. One normal stool.

11th September, 1949.—Discharged cured at request.

Case 3

A Hindu male, 15 years. Admitted 20th September, 1949, 9 p.m. History of vomiting and diarrhoea since 4 p.m. One member of the family died of similar condition a few days previously.

Condition on admission.—Dehydrated, collapsed, pulse imperceptible, urine not passed. Vomit and stool: only *T. vincenti* seen. No pathogens grown on culture.

On admission 800 cc. hypertonic saline intravenously given. Sulphaguanidine 4 tablets 2 hourly, mist. chloretone 4 hourly.

Treatment.—Hypertonic saline 500 cc. and normal saline 500 cc. intravenously with coramine.

30th September, 1949.—Condition same. Eight vomits and 8 stools in the night. Mapharside 25 mg. intravenously with 500 cc. normal saline given at 12 noon. At 8 p.m. no stool or vomit.

1st October, 1949.—Condition better. One normal stool. *T. vincenti* and *B. fusiformis* not seen in the stool.

4th October, 1949.—Discharged cured.

Ætiology

The outbreaks were definitely seasonal. In both the outbreaks studied, cases started coming in July at the end of summer, reached the highest incidence in September and gradually diminished by November, the beginning of winter.

The disease appeared to be essentially a sporadic one, unlike cholera. Cases came from scattered areas of the city, and except in one solitary instance not more than one member of the family was affected.

As is seen from table I, the disease can occur at any age and in both sexes. However, the

TABLE I

Age group in years	0-2	2-5	5-20	20-40	Over 40	Total
Male	6	5	16	23	4	51
Female	..	2	3	20	1	26
TOTAL	6	7	19	43	5	80

21st September, 1949.—Four vomits and continuous leakage from rectum since admission. Condition worse. Mapharside 40 mg. intravenously and 800 cc. normal saline intravenously given at 12 noon. 7.30 p.m. condition better. No vomit, one stool.

22nd September, 1949.—Condition improved. One normal stool. No *T. vincenti* seen in the stool.

25th September, 1949.—Discharged cured.

Case 4

A Hindu male, 10 years. Admitted 29th September, 1949, 6 p.m. Vomiting and diarrhoea since 2 p.m. Already had 20 vomits and same number of stools prior to admission.

Condition on admission.—Severe dehydration, collapse, pulse imperceptible.

Stool and vomit.—*T. vincenti* and *B. fusiformis* seen in large numbers.

maximum incidence appears to be in the age group of 20 to 40 years, which in our series accounted for 60 per cent of cases.

Causative agent.—This appears to be a thin spirillum with 3 to 7 irregular, delicate spirals, and long rods thick in the middle with tapering ends, both Gram-negative, morphologically identical with *T. vincenti* and *B. fusiformis*.

Mode of infection.—Appears to be obscure.

Signs and symptoms.—Disease is characterized by sudden and acute onset, with copious vomiting and profuse watery painless evacuations resembling typical rice-water stools. The diarrhoea may lead to continuous leakage from rectum. Dehydration and circulatory collapse appear very soon. These may be followed by muscular cramps, restlessness, and suppression of urine.

On examination, facial expression is pinched, with sunken eyeballs and cold clammy sweat

over forehead; skin dry and inelastic. Respiration rapid and shallow. Pulse rapid, feeble or imperceptible. Blood pressure very low.

Table II shows the percentage frequency of occurrence of some important signs and symptoms of cases.

TABLE II

Symptoms	Per-centage of cases	Symptoms	Per-centage of cases
Diarrhoea ..	100	Suppression of urine	35
Vomiting ..	96	Muscular cramps ..	28
Dehydration	92	Restlessness ..	20
Collapse ..	80	Temperature raised	5

Laboratory findings

Stool.—On naked-eye examination it is whitish, watery, and with a few flakes. There is no blood or mucus.

On microscopic examination a few pus and epithelial cells may be seen. No *E. histolytica*, ova, cysts, protozoa, *Vibrio cholerae* or Charcot-Leyden crystals are detectable. Stained smears show large numbers of *T. vincenti* and *B. fusiformis*. Culture: no intestinal pathogens are grown.

Vomit.—This also like the stool is whitish, watery, and with a few flakes. Stained smear shows *T. vincenti* and *B. fusiformis*.

Blood.—May show slight polymorphonuclear leucocytes. There is no anaemia; no malarial parasite.

Urine.—May show albumin in traces. Microscopic examination may show a few R.B.C.s, epithelial cells and casts.

As the bodies of fatal cases were not available to us post-mortem examination could not be done.

Differential diagnosis

The diagnosis of this disease rests entirely on the findings of *T. vincenti* and *B. fusiformis* in large numbers in stool as well as vomit, absence of other intestinal pathogens, and immediate response to arsenicals.

It has to be differentiated from cholera, choleraic type of dysentery, food poisoning, algid malaria, and irritant chemical poisoning. The first three can be ruled out by the absence of the specific organisms responsible for those conditions. In algid malaria blood examination will reveal the malarial parasite. In the last condition, there will be a definite relevant history and other signs.

Treatment

Immediate hospitalization is absolutely essential.

Non-specific.—On admission intravenous infusions of normal and hypertonic salines are given depending on the degree of dehydration. As many as 12 to 15 pints may be required in bad cases.

Measures to combat circulatory collapse in the form of injections of coramine, adrenalin, camphor in oil, and adrenal cortical hormone are given, with the usual hot-water bottles and blankets to keep the patient warm.

Gastric sedatives in the form of chlorotone and cocaine hydrochloride are also useful. To relieve restlessness, general sedatives like bromides and barbiturates may be used.

Specific.—Immediately the diagnosis is established by examination of stool or vomit, arsenic is administered in the form of mapharside in adults or acetylarsan in children. Stovarsol by mouth may be necessary in some cases, if complete relief of symptoms is not obtained by one injection of arsenical.

Complications and sequelae

1. Acute glomerulonephritis. This occurred in two cases, one in the arsenical series and another in the sulpha series. The condition appeared between 7 and 9 days after onset and cleared off completely in two weeks.

2. Papular urticarial rash with high fever occurred in one case on the 7th day and disappeared in 4 days' time.

3. Dermatitis with high fever occurred in one case on the 8th day which also cleared off with sealy desquamation of epithelium in five days.

4. Four deaths occurred in the sulpha series and two in arsenical series.

Discussion

The rôle played by *T. vincenti* and *B. fusiformis* in the pathogenicity of various necrotic lesions in the human body is still obscure. The finding of these organisms in deeper tissues does suggest some possibility of their assuming pathogenic character (Topley and Wilson, 1941), either by increase of their virulence or by decrease of local resistance of tissues. Menon has reported four cases in 1945 and one case in 1947 of intestinal fuso-spirochaetosis responding to arsenicals.

As already mentioned, we have had two outbreaks of acute gastro-enteritis, one in 1948 and the other in 1949. We could study 80 cases from these outbreaks, out of which 45 were treated by sulpha group of drugs and 35 with arsenicals. The disease clinically resembled cholera. Persistent efforts to isolate *Vibrio cholerae* or other pathogens proved futile. The constant presence of *T. vincenti* and *B. fusiformis*

in the stools as well as vomits led us to presume that the disease is not cholera, but a distinct clinical entity, possibly due to *T. vincenti* and *B. fusiformis*, giving rise to an acute inflammation of the gastro-intestinal tract.

The following distinguishing features of this disease entity were noticeable:—

1. The condition remained essentially sporadic, never assuming epidemicity though the outbreak continued for 3 to 4 months. The earlier cases were less severe than the later ones.

2. The disease did not appear to be very infectious. No case of contact infection occurred in spite of the fact that all our cases were kept in general wards.

3. In no case could *Vibrio cholerae* or other intestinal pathogens be isolated.

4. Almost all the cases showed *T. vincenti* and *B. fusiformis* in large numbers in stools as well as vomits.

occurred in fly season; so it is possible that flies may play some part in carrying the infection. Also the organisms normally present in the mouth are likely to be washed down into the stomach by the drinking of large quantities of water, where the diluted hydrochloric acid is unable to destroy them. They can multiply here and assume a pathogenic character, if there is some lowering of resistance of the mucous membranes. The incubation period is also not known. These require further investigations.

Summary

1. Two outbreaks of gastro-enteritis resembling cholera are described.

2. The disease appears to be a distinct clinical entity due to *T. vincenti* and *B. fusiformis*.

3. The specific effect of arsenicals as compared with sulphonamides in this disease is studied.

TABLE III

Time required for complete relief of symptoms in percentage of cases

Symptom	Treatment	0-6 hours, per cent	6-12 hours, per cent	12-24 hours, per cent	24-48 hours, per cent	2-5 days, per cent	Over 5 days, per cent
Vomiting	Arsenical ..	37	21	12	15	9	6
	Sulpha	12	18	56	14
Diarrhoea	Arsenical ..	30	28	15	12	12	3
	Sulpha	10	6	48	36
Complete cure ..	Arsenical ..	30	28	15	12	6	9
	Sulpha	66	34
Disappearance of <i>T. vincenti</i> and <i>B. fusiformis</i> .	Arsenical	85	..	6	9
	Sulpha	66	34
Total number of cases treated with:—1. Sulpha drugs ..		45					
2. Arsenicals ..		35					

5. Rather enormous quantities of saline were required to combat dehydration.

6. One injection of an arsenical practically cured the disease. Sulphonamides had either no effect or took a long time to bring about the same result.

As is seen from table III, within 24 hours of arsenical treatment, complete symptomatic relief occurred in 73 per cent of cases, and disappearance of organisms in 85 per cent of cases, whereas cases treated with sulphonamides took a much longer time.

The mode of infection, whether it is through food or water, is obscure. The outbreaks

We are indebted to Dr. S. K. Menon, Principal Medical Officer, Bikaner, for his valuable advice and kind permission to communicate this article. Our thanks are also due to the staff of the medical ward of the Prince Bijay Singh Memorial Hospitals for Men and Women, for their kind co-operation.

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TWO INSTANCES OF PROVED RABIES IN THE TIGER

By S. R. PANDIT

(Pasteur Institute and Medical Research Institute, Shillong)

SINCE all mammals and most vertebrates are susceptible to rabies, the tiger should be no exception, but although there are records in the statistics of Pasteur Institutes of instances of individuals mauled by leopards, etc., being treated with anti-rabies vaccine, the writer is not aware of proved rabies recorded in the Bengal tiger.

During the last few years there were two instances, at this Institute, of a positive microscopic finding in the brain of the Bengal tiger, the first in 1943 and the second during the current year. The brains were received at the Institute in a fixative—formol saline and methylated spirit, respectively. The biological test was therefore not possible, but with Neri stain, the routine stain employed at this Institute, well-developed and well-differentiated Negri bodies were seen microscopically in numbers, leaving no room for any doubt whatsoever. The existence of rabies, even in the King of the Jungle, emphasizes the enormity of the problem of eradication of rabies from this country, with so much of it stalking in wild life.

The first brain (in formol saline) was received in January 1943 from Dr. Hugh H. Smith, Chief Medical Officer, Nowgong Medical Association, Salana, Nowgong District, with the history that the tiger had 'severely mauled eighteen people in just over twenty-four hours but made no attempt to eat any of the victims'. He also stated that he had started anti-rabies treatment of the survivors, as he suspected rabies in the tiger. Because of the extreme interest of the case, I tried to obtain from Dr. Smith further details of the ravages of the animal, but failed. The following paragraph regarding the incident is extracted from my Annual Report of the Institute for 1943.*

'Among the specimens of brain tissue examined for evidence of rabies (*vide* table V) was that of a Bengal tiger, which was positive for Negri bodies. This is perhaps the first instance of a positive brain recorded in this species. The history is as follows: The animal severely mauled eighteen people in just over twenty-four hours "but made no attempt to eat any of the victims". It was later killed by shots in the shoulder in daylight near a railway station and the medical officer of the tea estate, who had already started anti-rabies treatment among the surviving victims, sent the

brain up for examination. This particular instance raises the issue as to the extent rabies is responsible for the man-eating propensity of tigers and, for the matter of that, for the unnatural and destructive behaviour displayed at times by other species such as the elephant. In such instances it is not only necessary to start anti-rabies treatment in the victims but also to submit the brain, where available, for examination at the Institute'.

The second instance of rabies in the same species occurred in April last, near Saikowaghat in the north-east frontier of Assam. The brain was sent by the assistant surgeon, fixed in spirit. At my request, the following information has been supplied by Dr. J. N. Palit, Civil Surgeon, north-east frontier, to whom I render thanks. The tiger was first seen at dusk on 13th April, 1950, in Garaimari village, 12 miles from Saikowaghat. On the night of 13th to 14th, between dusk and dawn, the animal had traversed at least 12 miles, terrorized the inhabitants of five or six villages and had attacked 14 persons, at least five heads of cattle and a dog, of whom one person and the dog were killed on the spot and two other persons died in hospital on the following day. The last person that was attacked in his house at Saikowaghat at 5 in the morning, managed to escape from the beast, shutting the door of the room behind him. The imprisoned animal was shot by a shikari an hour after, and measured 9 feet 4 inches.

[In this connection a reference to the article entitled 'Rabies in the Mongoose', *I.M.G.*, Vol. 68, 1932, p. 451, may be of interest. The following is the summary of the article:—

Three new cases of mongoose bite have been described. One positive mongoose's brain has been reported. Attention is drawn to a death presumably from mongoose bite in an untreated case. All mongoose bite cases treated and mongoose brains examined at Kasauli during the last 10 years, from 1922 to 1931, are tabulated.

The possibility of rabies coming into the domestic carnivora from the wild carnivora is discussed.

The suggestion is made to the effect that a mongoose bite should be treated as a serious bite.—EDITOR, *I.M.G.*

AN OUTBREAK OF PLAGUE IN AN EPIDEMIC FORM TREATED WITH STREPTOMYCIN AND SULFADIAZINE

By P. K. GHOSH, M.B.

(Seksaria Sugar Mills Ltd., Babhnai, Dist. Gonda)

AN epidemic of plague broke out last year at Babhnai and the vicinity, situated on the border of the two adjoining districts of Gonda and Basti (U.P.). This gave the writer an opportunity to treat plague cases on modern lines.

* Annual Report of the Pasteur Institute and Medical Research Institute, Shillong, for the year 1943—Assam Government Press.

The population of the locality is generally very backward in every respect. They still believe in the worship of deities who, they consider, are responsible for epidemics. Treatment in epidemic diseases is looked upon as a sacrilege and avoided at all costs, lest the wrath of the deity should spread the epidemic and take a heavy toll of human lives. Only those who are a little advanced and have visited cities come for treatment.

The disease started in the local market in late summer last year in bubonic form and remained localized and sporadic till the end of the year. Prophylactic inoculations were given among the residents of the locality by the writer and officers of the District Health Department during the quiescent stage of the malady, *i.e.* from August to November. But in spite of inoculations, cases occurred also among them. Adjacent villages were infected very soon, whence infection travelled far and wide and created panic among the people. Towards the end of November 1949, the disease flared up in an epidemic form.

When started, the epidemic was predominantly of bubonic variety but later on other types were also encountered. In a few cases cardiac embarrassment had been a taxing problem. There was no predilection for age, sex or community but the majority of cases came from the poor classes. Contrary to the usual involvement of the inguinal group of lymph glands, bubo in the upper part of the body were seen in no insignificant numbers. This is likely because the poor villagers mostly lie on the floor keeping their faces uncovered and sometimes the upper limbs also. Fleas have, therefore, more access to face and upper limbs for bite at night and the inguinal cases were presumably bitten during the day when they work and walk bare-footed and bare-legged.

Excepting the 6 deaths detailed below, all the remaining cases of the writer, 155 patients, receiving modern treatment made complete recovery without any debilitating after-effect. The period of suffering had been cut remarkably short—varying from a day to 5 days. Only one case, no. 10, who received no injection, took 10 days to recover. It was the adenitis that took some time to subside or suppurate even with iodex inunction. Only 4 cases required incision.

There were in all 9 moribund cases (case nos. 24, 25, 38, 39, 85, 86, 100, 114 and 118) with only 5 deaths among them. Case no. 25 died in an hour, no. 24 in 2 hours, no. 39 in 10 hours and no. 118 in 16 hours (could not take medicines) after being first seen and injected. Stimulants from the beginning including coramine, orally and parenterally, failed to show any response in them. Case no. 85 died on the 5th day of treatment due to heart-failure. All the 5 deaths among moribund cases

presented severe cardiac embarrassment. Four moribund cases, nos. 38, 86, 100 and 114, could be saved with strenuous efforts. Case no. 33 refused treatment after 12 hours, *i.e.* after the second injection, and died of cellulitis of neck after 48 hours.

The line of treatment (for adults) followed was :—

1. Injection of dihydro-streptomycin hydrochlor or sulfate or streptomycin-calcium chloride complex (as available)—

$\frac{1}{2}$ gm. in 0.5 cc. of 2 per cent sevicaine solution and 2.5 cc. normal saline—12 hourly.

No case required more than 2 injections, *i.e.* 1 gm. of streptomycin for defervescence and alleviation of symptoms and none except 3 patients agreed to take more after fever had gone and the alarming symptoms abated. Case no. 23 developed mumps 3 days after the second injection and he took two more injections, *i.e.* a total of 2 gm. Case no. 32 agreed to take 4 injections, as case no. 33 from the same house had died owing to discontinuation of treatment. Case no. 100 took 4 injections due to her moribund condition. A few cases got cured after a single injection.

Vestibular or auditory neurotoxicity, renal, allergic or any other reaction was not noticed in any case of the series. No untoward effect was seen on pregnancy.

2. Sulfadiazine—1 gm. (sulfatriad was substituted when sulfadiazine was not available).

Nicotinic acid (Pelonin)—50 mg.—4 hourly till defervescence—then 6 hourly and 8 hourly later on.

3. Alkaline mixture with digitalis, bromide, stimulants like spirit etheris, spirit ammon. aromat. and brandy according to individual requirement and coramine in suitable cases—4 hourly along with the tablets and at longer intervals later on.

The tablets were pulverized and suspended in the mixture with mucilage where it was feared that the patient would not be able to chew or swallow the tablets.

4. Sindol—1 powder or saridon—1 tablet. S.O.S. according to the severity of pain.

5. Local application of tincture iodine and belladonna plaster on the bubo with dry fomentations. Diet was restricted to milk, fruit juice and copious glucose water drinks.

Available literature on the treatment of plague does not give any clear-cut outline. Favourable effect of streptomycin on 3 plague cases was reported by Haddad and Valero (1948), and 5 cases by Karamchandani and Rao (1948). Seal (1949) also advocated the use of streptomycin.

Notable features

1. In a few cases bubo preceded pyrexia, in a few others the reverse was found, while in the majority both the complaints started together. Periglandular inflammation was considerable.

2. Prostration was marked in most cases and started from the beginning.

3. Pulse was almost always hurried, out of all proportion to the rise of temperature, soft and feeble.

4. Headache, bodyache and pain over the bubo were invariably severe.

5. Nausea and vomiting were present in a number of cases.

6. Suppression of urine did not occur except in one case (no. 86), even after administration of sulfadiazine.

Case no. 86 was moribund. She was first seen with anuria which yielded to suitable treatment. She had been previously treated by a Hakim.

7. Uncomplicated cases needed no after-treatment while complicated ones required it for recoupment of health.

8. No relapse occurred.

The data obtained in the present series of cases are analysed in tables I to IX:—

TABLE I
Showing plague cases monthwise

Month	Number of cases	Cures	Percentage	Deaths	Percentage	REMARKS
Before November 1949	1	1	100.0	Nil	0.0	Cases showed a steady rise up to April. There was a sharp fall in May, when atmospheric temperature rose very high (112°F. in shade) accompanied with strong hot westerly wind.
November 1949	1	1	100.0	Nil	0.0	
December 1949	4	4	100.0	Nil	0.0	
January 1950	18	17	94.4	1	5.6	
February 1950	31	28	90.3	3	9.7	
March 1950	33	32	97.0	1	3.0	
April 1950	60	59	98.0	1	1.7	
May 1950	7	7	100.0	Nil	0.0	
TOTAL	155	149	96.1	6	3.9	

TABLE II
Showing plague cases sexwise

	Number of cases	Uncomplicated cases	Complicated cases	Percentage of complicated cases	Cures	Percentage	Deaths	Percentage	REMARKS
Male	86	60	26	30.2	83	96.5	3	3.5	Females showed a higher percentage of complication.
Female	69	39	30	43.4	66	95.6	3	4.4	
TOTAL	155	99	56	36.2	149	96.1	6	3.9	

TABLE III
Showing plague cases comparatively between inoculated and non-inoculated persons

	Number	Cures	Percentage	Deaths	Percentage	REMARKS
Inoculated	57	55	96.5	2	3.5	Non-inoculated persons showed higher case incidence and higher mortality rate.
Non-inoculated	98	94	95.8	4	4.2	
TOTAL	155	149	96.1	6	3.9	

TABLE IV
Showing plague cases agewise

Age group	Number of cases	Cures	Percentage	Deaths	Percentage	REMARKS
Up to 5 years ..	5	5	100.0	Nil	0.0	Cases over 5 to 15 years age group showed the highest mortality. All deaths had been among moribund cases and the death took place within 16 hours. Lowest age—3 years. Highest age—70 years —both cured.
Over 5 to 10 years ..	18	15	83.3	3	16.7	
Over 10 to 15 years ..	14	13	92.9	1	7.1	
Over 15 to 20 years ..	9	9	100.0	Nil	0.0	
Over 20 to 25 years ..	27	26	96.3	1	3.7	
Over 25 to 30 years ..	17	17	100.0	Nil	0.0	
Over 30 to 35 years ..	23	23	100.0	Nil	0.0	
Over 35 to 40 years ..	17	17	100.0	Nil	0.0	
Over 40 to 45 years ..	4	4	100.0	Nil	0.0	
Over 45 years ..	21	20	95.2	1	4.8	
TOTAL ..	155	149	96.1	6	3.9	

TABLE V
Showing distribution of bubo

Group of glands involved	Number of cases	Cures	Percentage	Deaths	Percentage
Right inguinal group	44	43	97.8	1	2.2
Left inguinal group	42	42	100.0	Nil	0.0
Bilateral inguinal groups	4	4	100.0	Nil	0.0
Right axillary group	9	8	88.9	1	11.1
Left axillary group	16	15	93.7	1	6.3
Bilateral axillary groups	0
Right cervical group	7	6	85.7	1	14.3
Left cervical group	6	5	82.3	1	16.7
Bilateral cervical groups	2	2	100.0	Nil	0.0
Other groups	6	5	83.3	1	16.7
Multiple groups	15	15	100.0	Nil	0.0
No bubo	4	4	100.0	Nil	0.0
TOTAL ..	155	149	96.1	6	3.9

TABLE VI
Showing types of plague cases

Types	Number	Cures	Percentage	Deaths	Percentage	REMARKS
Uncomplicated ..	99	98	99.0	1	1.0	* Other types (a) Cardiac type—2 cases with 1 death. (b) Complicated with enteric (19 days)—1 case—report published in I.M.G., December 1949. (c) Complicated with puerperium—1 case—saved.
Broncho and pneumonic ..	19	19	100.0	Nil	0.0	
Meningeal ..	17	14	82.4	3	17.6	
Cerebro-bronchial ..	4	4	100.0	Nil	0.0	
Septicæmic ..	5	4	80.0	1	20.0	
Diarrhœic ..	5	5	100.0	Nil	0.0	
Cellulocutaneous ..	2	2	100.0	Nil	0.0	
Other types* ..	4	3	75.0	1	25.0	
TOTAL ..	155	149	96.1	6	3.9	
Moribund cases ..	9	4	45.5	5	55.5	

TABLE VII
Showing duration of treatment

Days	Number of cases	Cures	Deaths	REMARKS
Less than 16 hours ..	5	1	4	As 4 out of 6 deaths occurred between and 16 hours of starting treatment, it appears, duration of treatment had no effect on mortality.
1 day ..	20	20	Nil	
2 days ..	89	89	Nil	
3 days ..	30	29	1	
4 days ..	8	8	Nil	
5 days ..	2	1	1	
10 days ..	1	1	Nil	
TOTAL ..	155	149	6	

TABLE VIII
Showing duration of illness

Duration of illness	Number of cases	Cures	Deaths	REMARKS
Less than 1 day	1	1	Nil	Duration of illness before treatment was started had practically no effect on mortality.
1 day ..	39	39	Nil	
2 days ..	24	22	2	
3 days ..	36	35	1	
4 days ..	27	25	2	
5 days ..	11	11	0	
6 days ..	6	5	1	
7 days ..	8	8	0	
10 days ..	1	1	Nil	
12 days ..	1	1	Nil	
19 days ..	1	1	Nil	
TOTAL ..	155	149	6	

TABLE IX
Showing cases familywise

	Number of families	Number of cases	Cures	Deaths	REMARKS
Individual cases	104	102	2	Number of cases in a family was no factor in influencing mortality.
Families containing 2 cases ..	10	20	17	3	
" " 3 " ..	2	6	6	Nil	
" " 4 " ..	1	4	3	1	
" " 5 " ..	2	10	10	Nil	
" " 11 " ..	1	11	11	Nil	
TOTAL	155	149	6	

Summary

1. An epidemic of plague is described.
2. An outline of treatment followed is given.
3. A series of 155 plague cases is discussed.

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INSULIN RESISTANCE IN DIABETES PATIENTS

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CASES of diabetes requiring extraordinarily large doses of insulin have been met with from time to time. On detailed clinical investigations being made on these cases, some very striking results have been obtained. In some of them it was found that it was not possible to

stabilize them even with extremely high doses of insulin and it appeared as if they were 'insensitive to insulin'.

Insulin-resistant cases of diabetes

Thorough clinical and laboratory investigations were made on all these cases under hospital conditions. From the clinical data which were obtained from the different lines of treatment adopted in the different types of cases, they may be divided into the following broad groups:—

(1) Cases of diabetes with hyperthyroidism

These cases were usually found to be extremely resistant to insulin. On clinical investigation it was revealed that a condition of hyperthyroidism existed in them along with the diabetic condition. The persistence of marked hyperglycaemia in spite of very big doses of insulin was found to be due to a co-existing condition of thyrotoxicosis which was confirmed by clinical tests. In some of these cases the condition was further complicated by the presence of toxæmia and hepatitis.

The effect of the hyperthyroid condition in these cases of diabetes appeared to be two-fold:

(a) Decreased glycogen storage and increased glycogenolysis.

(b) Antagonism to insulin action.

That a condition of hyperthyroidism interferes with the action of insulin was confirmed by animal experiments by the writer in 1924. In this work it was proved that the Albino-Himalayan type of rabbits, which are usually met with in this country, were very resistant to insulin action as compared to the Belgian hare type of rabbits and thus they were unsuitable for insulin standardization tests. The cause of insulin resistance in the Albino-rabbits was found to be due to a condition of a comparative hyperthyroidism existing in these animals as compared with the Belgian hare type of rabbits.

Treatment with thiouracil.—Some of the insulin-resistant cases referred to above were treated with methyl-thiouracil (M&B) with satisfactory results. The resistance to insulin in most of these cases (particularly in the two cases described below) decreased considerably and they could be stabilized with a very much smaller dosage of insulin, as will be evident from the synopsis of the results given.

Case 1.—J. S., age 50 years (P.P 1), admitted on 5th March, 1948.

Date	Blood-sugar fasting level, per cent	Total sugar excretion in urine in 24 hours, gm.	Body-weight, lb.	Treatment	REMARKS
5-3-48	Diet C = 120 gm. P = 70 " F = 120 "
6-3-48	0.340	110	102	Insulin— 60 units morning 30 units evening	90 units of insulin continued for 10 days did not appreciably reduce either the blood-sugar level or the sugar excretion in urine. The patient was reduced by 2 lb.
8-3-48	0.336	112	100	Methyl-thiouracil tablets (M&B) (0.2 gm. each) four times daily or 0.8 gm. daily were started.	This evidently had a marked effect on both the blood-sugar and the glucose excretion which were reduced considerably after 10 days. The weight was increased.
26-3-48	0.220	42	104	The dose of insulin was reduced to 60 units per day. Methyl-thiouracil tablets were continued in doses of 0.8 gm. daily.	In spite of reducing the dose of insulin the reduction of both blood and urine sugar continued.
3-4-48	0.150	15	104	The dose of insulin was further reduced and P.Z.I. given in doses of 30 units once daily.	In spite of further reduction of insulin dosage the blood-sugar came down almost to the normal level and the urine became sugar-free.
10-4-48	0.120	Nil	..	The patient left hospital with instructions to follow diet along with 20 units of insulin and 0.4 gm. of methyl-thiouracil daily. He reported again on 17-4-50 when the blood-sugar was found to be 0.108 per cent and the urine free from sugar.	

Case 2.—S. R., age 26 years (P.P. 8), admitted on 5th July, 1948.

The results are evidently encouraging and more cases are worth following up.

also been shown that cystine and cystine precursors like methionine are likely to play an important part in the biological synthesis of insulin. Lack or absence of these precursors is

Date	Blood-sugar fasting level, per cent	Total sugar excretion in urine in 24 hours, gm.	Body-weight, lb.	Treatment	REMARKS
5-7-48	Diet. C = 120 gm. P = 70 " F = 120 "
6-7-48	0.120	115	81	Insulin 60 units twice daily (120 units per day).	No evident change either in the blood-sugar level or in the total sugar excretion in urine was noticed in spite of such a high dose of insulin.
13-7-48	0.117	149	83	The dose of insulin was kept the same but methyl-thiouracil in doses of 0.8 gm. per day was started.	Considerable reduction in the blood-sugar level and sugar excretion occurred within 7 days.
20-7-48	0.290	87	84	Insulin 120 units per day and methyl-thiouracil in 0.8 gm. per day was continued.	Further improvement in both blood-sugar and sugar excretion was evident.
27-7-48	0.180	25	85	The dose of insulin was now reduced to 60 units per day. Methyl-thiouracil continued in the same dose.	In spite of the reduction of the insulin dosage to half, the improvement continued.
3-8-48	0.140	Traces	85	The dose of insulin was further reduced to 40 units daily but methyl-thiouracil was continued in the same dose.
10-8-48	0.160	8	No change in the treatment was made though both the blood-sugar and the total sugar excretion showed slight increase.
17-8-48	0.130	Nil	86	The dose of insulin was now reduced to 20 units daily. Methyl-thiouracil continued in doses of 0.6 gm. daily.
24-8-48	0.108	Nil	86	Treatment discontinued

(2) Lack of glutathione

It has recently been shown that the injection of a large dose of glutathione immediately preceding a diabetogenic dose of alloxan completely protected the rats from diabetes. Glutathione, which is a normal constituent of the cells, is said to react with alloxan and reduce it to dialuric acid which is not diabetogenic. Cystine and some other substances of the sulphhydryl group are also said to react with alloxan in a similar way.

Whatever may be the mechanism by which alloxan selectively destroys the beta-cells of the pancreas it is clear that glutathione of the body influences the susceptibility of the animals to alloxan diabetes.

It is also an interesting fact that insulin contains a large percentage of cystine. It has

believed to hamper the process. It therefore appears that these substances are likely to play an important rôle in the diabetes therapy. Methionine, in addition, plays an important part in detoxication by the liver and this fact also takes an important part in insulin resistance.

With a view to finding whether feeding with methionine is likely to increase the glutathione content of the blood and help in improving the diabetic condition and making the patient less resistant to insulin the following clinical experiment was tried. Only a few cases have so far been treated and the typical results obtained from one of them have been incorporated in this paper. They are encouraging.

Case 3.—S. N. C., a Hindu male, age 37 years, (Lukis 7) diabetes of long standing and of moderate severity, admitted on 21st March.

1950. The patient was used to take very big doses of insulin continuously for the last 7 years but even then the control of his hyperglycæmia and glycosuria was unsatisfactory.

When admitted, the patient had a fasting level of blood-sugar of 0.450 per cent and a total urinary excretion of 163 grammes per day; 80 to 100 units of insulin per day failed to control his hyperglycæmia or glycosuria.

Remarkable results were however obtained when methionine was started in fairly big doses along with the same dose of insulin, and it was later found that the insulin injections could be drastically reduced to one daily.

A synopsis of the results is given below :

It is therefore essential that in all these cases the source of infection should be sought for and brought under control as soon as possible. It will then be found that the need for insulin will be also greatly reduced. The possibility of an infection somewhere should always be kept in mind in the treatment of insulin-resistant cases.

A rather remarkable case of insulin resistance caused by bad pyorrhœa is cited below :—

Case 4.—J. S., an Anglo-Indian girl, age 18 years, blood-sugar (fasting level) 0.370 per cent, urine sugar + + +, acetone + +, diacetic acid nil. On examination of the teeth oral infection with a bad pyorrhœa was elicited.

Date	Blood-sugar fasting level, per cent	Total sugar excretion in urine in 24 hours, gm.	Treatment	REMARKS
21-3-50	0.450	163	Insulin 60 units in 2 doses was started.
15-4-50	0.390	130	Insulin was continued, 100 units daily.
27-4-50	0.395	130	Methionine 2 tablets (0.2 gm. each) thrice daily (i.e. total 1.2 gm. daily) was started and the injection of insulin continued in doses of 100 units daily.
11-5-50	0.300	90	Methionine 2 tablets thrice daily with 100 units insulin daily was continued.
18-5-50	0.200	15	Dose of insulin was reduced to 60 units daily. Methionine continued in the same dose.	A definite improvement was noticed both in the fasting blood-sugar level and the total urinary sugar excretion in spite of the reduction of the dose of insulin.
25-5-50	0.175	Traces	Further reduction in the dose of insulin (50 units daily) was made. Methionine tablets were continued in the same dose.	Marked improvement occurred. The blood-sugar came down to normal and the urine free from sugar.
30-5-50	0.080	Nil	The patient was discharged with instructions to continue insulin in smaller doses and also continue methionine 2 tablets b.d. for 10 days.	

In view of the results obtained similar trial should be made in other resistant cases of diabetes.

(3) Acute and chronic infections

It has been found that acute and chronic infections are the usual causes of insulin resistance in a large number of cases of diabetes, though temporarily. Infection or toxæmia has been found to block insulin action. This means that the amount of glucose utilization per unit of insulin becomes severely retarded in the presence of a severe infection or toxæmia with the result that the hyperglycæmia increases gradually in spite of big doses of insulin.

On admission the patient was put on hospital diet consisting of C. = 120 gm., F. = 120 gm., P. = 70 gm., and it was found that even a dose of 100 units of insulin per day was unable to control properly the diabetic condition.

The patient was sent to the dental department and a total extraction of the teeth was done under gas. From the 3rd day onwards the patient became sugar-free and the blood-sugar level came down considerably. The requirement of insulin became progressively less and on the 12th day after the teeth extraction it was found that the condition could be controlled on diet alone without insulin.

(4) *Disturbance of the liver function*

In some cases of diabetes the requirement of very high doses of insulin was found to be due to disturbances of the liver function such as hepatitis and also chronic passive congestion as a result of cardiac decompensation, temporarily causing a marked disturbance in the glycogenic function of the liver. When these factors gradually return to normal, the insulin requirement was found to be markedly lowered.

Case 5.—N. R. C., diabetes with marked jaundice. Fasting blood sugar level 0.380 per cent, urine sugar + + + +, acetone + + +, diacetic acid + + +. X-ray examination revealed gallstones.

A dose of 120 units of insulin per day was unable to control the hyperglycemia or the ketosis. As much as 200 units of insulin had to be given to control the hyperglycemia, acidosis and the glycosuria and to make the patient fit for surgical operation.

The patient was operated on and a cholecystectomy done. Two large stones were found in the common bile duct. For about 10 days following the operation the big doses had to be continued after which the insulin requirement was found to become gradually less and less to 24 units daily.

(5) *Allergy*

In a certain number of individual cases it was found that allergy due to insulin or to other causes was responsible for sudden and persistently rising hyperglycemia sometimes very difficult to control. When these cases were desensitized by proper methods, the condition improved. Such cases are comparatively rare.

Summary and conclusions

Apart from the usual causes of uncontrollable hyperglycemia in spite of extraordinarily high dosage of insulin, such as acute and chronic infections, disturbance of liver function, allergy, etc., two outstanding causes of insulin resistance were found to be (a) condition of thyrotoxicosis co-existing with diabetes and (b) lack of glutathione content of blood in diabetic subjects.

Treatment of thyrotoxicosis with thiouracil has been found to make the patient less resistant to insulin and reduce the insulin requirement drastically in most cases.

Some cases of diabetes with a lowered glutathione content of blood were found to be extremely resistant to insulin. Feeding with methionine in these cases had a marked effect on the insulin requirement, which could be substantially reduced or even stopped.

Oral administration of methionine has also been found to lessen or even eliminate the need of insulin in cases of diabetes not necessarily resistant to insulin.

HYDROPHOBIA IN INDIA

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History.—The earliest reference that we have been able to find in Hindu mythology with regard to dogs and their association with death is in the Vedic period. In Atharva Veda, Yama, the God of Death, is described as being attended by dogs, his constant companions and emissaries of death: 'Broad-nosed and brown, the messengers of Yama, greedy of lives, wander among the people' (Macdonell, 1825).

Strangely enough there does not appear to be any mention of a rabies-like disease in the Bible, though it seems probable that the two she-bears which killed 42 children who taunted the prophet Elisha, because of his baldness, were rabid (2nd Kings II, 24, 25).

The following historical details have been gleaned from a most crude study of the subject in a book on rabies by G. Fleming, published in 1872 by Hall and Chapman: Rabies and hydrophobia were well known to the ancient Greeks and Romans. Plutarch asserts that hydrophobia was first observed in mankind in the days of Aesclepiadæ, the descendants of the god of medicine Æsculapius, by his sons Podalirius and Machaon, who spread through Greece and Asia Minor as an order of priests, prophets and physicians, preserving the results of the medical experience acquired in the temples as a hereditary secret. The mythical story of Actæon, who was torn to pieces by his hounds because he had surprised Diana and her attendants bathing, probably had its origin in the circumstance that a famous hunter was destroyed by his own pack of dogs which became rabid. In the Iliad, Homer is thought to refer to rabies when he mentions the dog-star, or Orion's dog, as exerting a malignant influence upon the health of mankind. Aristotle, in the fourth century B.C., states 'Dogs suffer from "lytta" which produces madness, and they infect every creature which they bite, except man'. Celsus, although probably not even a medical man, in about A.D. 30, appears to have made a special, and a remarkably accurate, study of rabies and to have fully recognized that the virus was present in the saliva. Celsus strongly recommended cauterization, burning, cupping and also sucking the wounds of those bitten by rabid animals, making special mention of the fact that it was essential for the safety of the operator to have no sores or abrasions on his lips or in his mouth. He recommended the actual cautery and said that if the wounds were so situated that they could not be burnt then medicines which violently

corrode should be used. Celsus described hydrophobia as 'a most wretched disease, in which the sick person is tormented at the same time by thirst and the fear of water and in which there is but little hope'.

There is nothing especially noteworthy in the history of rabies subsequent to these early reports, for knowledge of the subject remained more or less stationary till the classical work of Pasteur which led to the introduction of antirabic vaccines.

Incubation period.—There is no other acute infectious disease that we know of in which the incubation period is so variable, or dependent on so many different factors. The virulence of the particular strain of virus; the quantity of saliva deposited on the wounded surface, or inoculated into the bite; the tissue bitten, whether rich in nerve supply or not; the species of biting animal; the distance of the site of the bite from the brain; non-specific treatment with cauterizing agents; specific treatment with vaccines and sera; all these play a part in regard to the incubation period and may modify it. In particular we draw attention to the incubation period in bites of the head and face. The short incubation period in these cases is attributed to the nearness of the wound to the brain and, in general, we agree with this obvious explanation, but it must also be borne in mind that such bites are likely to be inflicted by particularly ferocious, large and powerful animals, which either knock the patient down and inflict grave injuries, or leap up to bite, thus causing lacerated wounds on bare skin and on tissues which are richly supplied with nerve filaments. These bites are, therefore, more likely to cause infection and in a shorter period of time than bites on the leg and other less enervated tissues such as the trunk.

The disease generally manifests itself between the first and second month after the bite. Of 1,321 cases of hydrophobia treated at Kasauli and its centres, only 78 cases, distributed as follows, had an incubation period of less than 21 days:—

Number of cases of hydrophobia with an incubation period of less than 21 days

Total number of cases of hydrophobia analysed in this series	Incubation period (days):										
	11	12	13	14	15	16	17	18	19	20	
1,321	2	0	3	3	5	14	11	16	12	12	

An incubation period of less than 15 days is most exceptional but there is no reason to doubt that cases with such a short incubation period do occur. At the same time it must be borne

in mind that the doctor is wholly dependent on patients for histories recorded, and that these are not always reliable. For example, in our own experience, we know of a case of hydrophobia in an ignorant village woman, who stated that she had been bitten only 10 days before. Asked if the dog had attacked any one else she replied that she and two others had been bitten by it at the same time and that both the others had died of hydrophobia. Closer interrogation showed that she had been bitten quite 2 months earlier than she had stated in the first place. The longest authenticated incubation period on record was reported by Iyengar (1935). This was in a child aged 10½ years who developed hydrophobia 3 years, 2 months and 21 days (1,176 days) after having been bitten by a street dog on the hand and chest. The child had been treated with 5 cc. of 1 per cent carbolyzed vaccine for 14 days. Cases of hydrophobia developing more than a year after exposure to infection are rare, and such incubation periods must be viewed with a certain degree of suspicion, always keeping in mind the possibility of a subsequent infection which may have been responsible for the disease. In the case reported by Iyengar, however, this possibility was carefully considered and ruled out.

An analysis of a series of 323 cases of hydrophobia shows that the average incubation period for head, neck and face bites is 34 days, for bites on the upper extremity 46 days and for bites on the lower extremity 78 days. In this series the incubation period was a month or less in 33 per cent, between one and 3 months in 49 per cent, between 3 and 6 months in 13 per cent, between 6 and 12 months in 3.5 per cent and over 12 months in 0.5 per cent of cases. The incubation period is somewhat shorter in infants and children than in adults. Thus, in the above series it was 52 days for those 15 years of age and under, and 67 days for those over 15 years of age. This is, in part, due to the fact that children are likely to be more severely bitten than adults and to be more frequently bitten on the face.

Prognosis.—Mortality in treated cases in India, in those actually bitten, is in the neighbourhood of 0.3 per cent. Of untreated persons (bitten by rabid animals but not given specific treatment) the chances are that about 80 to 90 per cent would escape infection. In untreated cases we may say that if the patient survives 2 months after exposure his chances are good; if he survives 3 months he is unlikely to develop hydrophobia, and beyond this period he may be regarded as almost free from danger, though no guarantee can be given until at least a year has elapsed from the date of bite. In treated cases the incubation period, as previously pointed out, may be prolonged as evidenced by our own experience and the case reported by Iyengar. This is also borne out by

experimental evidence in animals in which those treated but succumbing to the disease generally have a longer incubation period than untreated controls.

Symptoms.—The classical symptoms of hydrophobia are too well known to require detailed description, and may be found in most text-books. We, therefore, do not intend to describe them but draw attention to one or two points of practical importance. One should not ask a person suffering from hydrophobia to drink water. The patient is well aware that water is being given to him for the sake of deliberately evoking a spasm, and he naturally—and rightly—resents such behaviour on the part of a doctor. One should offer him 'medicine' which may consist of water coloured with a little tincture of cardamom compound or similar substance. Under the impression that he is being treated the patient will accept this, and one may take the glass from him the instant the characteristic spasm clinches the diagnosis. Watch the patient carefully when he attempts to drink: it will be seen that his hand trembles as he is about to seize the glass and this trembling increases as he raises it to his mouth so that some fluid is usually spilt as he commences to drink. At the same time the head may be jerked back, and the patient seems to be trying to drink in too great a hurry. The muscles of the throat contract, and as he removes the glass from his mouth, he struggles to swallow and to breathe.

In hysterical conditions, in which the patient believes that he is suffering from hydrophobia, the picture is very different. There is usually a much exaggerated fear of water and the patient may refuse to attempt to drink. When persuaded to do so his hand does not tremble as he seizes and raises the glass. He may then throw the water away instantly, or if he takes a mouthful, he usually spits it out immediately without making any attempt to swallow it.

The symptoms of hydrophobia are modified by the temperament of the patient. Most patients are able to control themselves fairly well, but we have known a professional wrestler who broke down the wooden door of the room in which he was confined, with the leg of his bed. Brandishing this weapon he entered a ward and would undoubtedly have done some one an injury had it not been for the presence of mind of a colleague who threw a glass of water on his face and quickly disarmed him while he was struggling in the throes of the spasm brought on by the drenching. On the other hand we have seen a little Sikh lad, 6 years of age, who had such self-control that, to oblige the doctors under training who had not previously seen a case of hydrophobia, he took several spoonfuls of water; when praised by them for his bravery, of his own accord he asked for more water and again took several sips of it. This child was excessively talkative and

almost gave the impression of showing off. He was bright, evinced no signs of anxiety and sucked glucose sweets readily; and the attendant doctors were much inclined to question the correctness of our diagnosis till the patient died 4 hours later. This, and many other cases of hydrophobia in children which we have seen, leads us to believe that the disease is not as agonizing a one as it appears to be in adults, who are aware of the fatal issue. It is this certain knowledge of impending death that so terrifies and adds to the physical distress of adults, but the child, mercifully unaware that he is about to die, seems to suffer no more than he would in many other acute diseases.

A point worth remembering, and seldom mentioned in books, is that the symptom of 'hydrophobia' frequently passes off in patients who survive for more than three days. We have known this to occur in four cases and draw attention to the disappearance of this, the most characteristic symptom of the disease, which is apt to lead the inexperienced medical attendant to believe that the patient is recovering, or to doubt the correctness of his diagnosis in the first instance.

Hydrophobia-phobia, a neurosis in which an exaggerated fear of hydrophobia is manifested, is not uncommon and we have seen several cases. The following is an example of this type of neurosis: An educated well-to-do gentleman, aged 35 years, recently came to Kasauli, after having put through five long-distance telephone calls within two days, to ask if he should be treated because a dog in the street had brushed against him; saliva may have been left on his trousers, he may have contaminated his hand with the saliva; and shortly after the dog had touched him he sucked a lozenge without having first washed his hands. There was no particular reason to suspect that the dog was rabid; it had not attempted to bite him or any one else on the road at the time, yet this patient worried so much that a doctor (not at Kasauli) was induced to give him antirabic treatment. A few weeks later the patient came back to the Institute at Kasauli demanding further treatment because, according to him, the doctor may have used the same iodine swab on him as was used on another person getting prophylactic injections and he feared that this other person may have been developing hydrophobia.

Most of these cases of hydrophobia-phobia have already undergone a course of treatment but their fears lead them to demand more treatment. Their misgivings can generally be allayed by one who does not hesitate to claim expert knowledge and who impresses the patient with his own self-confidence. In dealing with such a case it is best to tell the patient that he is suffering from a phobia; explain that such phobias are not uncommon; state that you have known of several others in like condition; assure him that hydrophobia is not an easily

acquired disease and that the treatment already given has been more than ample; emphatically declare that his fears are groundless and resolutely refuse to give him more treatment. In spite of this, some patients will stubbornly cling to their pet phobia and these should be referred to a psychiatrist. Often the phobia is deliberately fostered as a substitute for other causes of worry. We recall the case of Mrs. X., a young woman who wrote lengthy letters daily to the Director of a Pasteur Institute, sent him numerous telegrams and put through telephone calls to his office and residence at all hours of the day and night. She worried over such absurd possibilities as acquiring hydrophobia by stepping on a banana skin which, according to her, may have been thrown away by some one who had hydrophobia or which may have been contaminated by a stray dog. Investigation showed that this lady had been recently divorced, that she had been deprived of the custody of her child, and that she was leading an immoral life; and hence her phobia which was adopted as an escape from her real woes.

Prophylaxis and treatment.—All bites from animals, particularly if unprovoked, should be regarded as dangerous and the following local treatment should be carried out immediately. Wash the wound with soap and water. Any soft soap will do, provided it is used freely and reaches the depths of all pockets of wounds. Soap not only helps to wash away infective materials but will neutralize the virus of rabies in tissues with which it comes in contact. It is also advisable to use a strong jet of water from the tap while washing with soap, as the mere mechanical action of the stream may remove the virus.

After the wound has been thoroughly washed the patient should go to the nearest dispensary where the wound should be cauterized with pure carbolic acid. In the case of a deep penetrating wound a probe dipped in carbolic acid should be used to ensure that the wound is cauterized to its entire depth. Immediately after the application of carbolic acid, the wound should be swabbed with a pledget of cotton-wool dipped in absolute alcohol, rectified spirit, or methylated spirit in order to prevent excessive cauterization of the tissues by carbolic acid. Some authorities prefer fuming nitric acid to carbolic acid. We do not recommend it as it is no more effective than phenol and causes considerable pain.

Recent work, in experimental animals, suggests that the application of tincture of iodine is as effective as cauterization, and this of course would have the advantage of not causing scarring. For face bites involving the eyelids, nose and mouth, iodine is therefore recommended.

In cases where there is no reason to suspect that the biting animal was rabid, and when the animal is under observation, commencement of

specific prophylactic treatment with antirabic vaccine should be left to the discretion of the medical officer in-charge of the antirabic centre. If the animal remains alive and well for the conventional ten days' period it can be taken for granted that the saliva was not infective at the time of biting and antirabic vaccine treatment is not necessary in such cases. In bites of the head, face and neck, it would be advisable to commence treatment immediately, and to take no risk. Every day that the biting animal remains alive and well, lessens the chances of its having been in an infective stage when it inflicted the bites. Treatment may, therefore, be discontinued after the first three injections, provided of course that the animal shows no signs whatever of sickness during this period. Treatment should of course be recommended on the first sign of illness of the animal within 10 days' period of observation. If the animal develops rabies it is almost sure to die within two or three days of the onset of noticeable symptoms.

In all other cases where the biting animal is not traceable or when there is reason to suspect that it is rabid, the patient should be sent immediately to the nearest antirabic centre for treatment.

In the present stage of our knowledge the actual treatment of hydrophobia literally amounts to euthanasia. Scores of drugs have been tried, including indigenous 'sovereign remedies', the latest antibiotics including aureomycin and chloromycetin, various sulphur compounds and their combinations, and one and all have proved equally worthless in the treatment of hydrophobia.

In the absence of a cure the doctor to-day views a case of hydrophobia with utter despair, and resorts to large doses of sedatives, such as morphia, to bring the disease to a speedy termination. This attitude should not be encouraged. Recently, Sulman (1950) recorded two cases of 'abortive' hydrophobia one of which occurred in 1921 and the other in 1948. The second case was in a boy, 9 years of age, who developed hydrophobia six weeks after he was bitten by a rabid cat. The claim that this was a genuine recovery from hydrophobia must be accepted with reserve, for proof of the diagnosis could only be established by the successful passage of his saliva (which unfortunately, but understandably enough, was not done during the acute stage of the disease). Nevertheless, the characteristic symptoms described by an experienced worker on rabies are highly suggestive of hydrophobia, and hysterical simulation of hydrophobia would be unlikely in so young a patient; besides, the incubation period of six weeks is against a probability of hysteria. If then this recovery is genuine it shows that hydrophobia may be curable. If the patient can be treated in a well-equipped hospital, we suggest that hyper-immune serum, curare or

tubercine, and an iron lung may be of use. Furthermore, judging by histological findings in the brains of animals which have died of rabies, damage to brain tissues does not appear to be greater than say in tetanus or cobra-venom poisoning, from both of which recovery may be complete. Accordingly, should it ever be possible to cure hydrophobia, there is no reason to adopt the pessimistic belief that this would leave the patient with a permanent disability due to brain injury.

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SEROLOGICAL TECHNIQUE :

IMMUNOTHERAPY (contd.)

IMMUNIZATION AGAINST RABIES

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For protection of man after bite from a rabid animal

The vaccine.—The Semple vaccine is used in India and in most other countries. In India, it is a 5 per cent suspension of the brain of a sheep, paralysed after infection with fixed virus of rabies through cisterna puncture. The brain is removed with sterile precautions, ground into 8 per cent suspension with normal saline and phenolized to obtain a concentration of 1 per cent of the antiseptic. The phenolized suspension is left at 37°C. for 24 hours. Next day enough normal saline is added to reduce the brain substance to 5 per cent (and the phenol to about 0.6 per cent). The suspension is then tested for the presence of phenol and for bacterial sterility. The phenol should produce colour with tinct. ferri perchloride (B.P.) and bacteria should be absent in an aerobic and an anaerobic culture examined 24 hours later.

The credit for the development of this vaccine belongs to the Pasteur Institute of India, Kasauli, which functioned from 1900 to 1939. Major Semple (later Sir David) of the R.A.M.C. was its first Director. He studied the rival methods then in use in Europe and came to the conclusion that a 2 per cent suspension of the infected rabbit's brain and cord rendered inert with 1 per cent phenol at 37°C. for 24 hours and then diluted with equal volume of saline to yield a 1 per cent suspension (with 0.5 per cent phenol) was as effective as any other preparation. The other methods were : (1) The use of original 1 per cent suspension of cords dried for varying periods, at Paris. The first suspension was made from a cord dried for 14 days, the second from a cord for 13 days, and so on until a cord dried for 1 day was

reached. This was treated in 1885, the first case, Joseph Meister, aged 9, bitten in 14 places. (2) The use of varying dilutions of a fresh cord suspension. The treatment was continued with a weak dilution and ended with a strong dilution. (3) The use of a constant weak dilution of a fresh cord suspension.

Then, after Semple's time, came the trial of other vaccines. Brains of rabbits paralysed with fixed virus were left in ether, ground up into a 5 per cent suspension and used straightway. The freedom of the suspensions from bacteria could not be guaranteed.

Then came the idea of using a 5 per cent suspension, instead of the 1 per cent suspension, of the infected brain, in making the ordinary phenolized vaccine. By trial and error it was established that 1 per cent phenol could render inert with certainty an 8 per cent suspension of the infected brain : hence the 8 per cent suspension and 1 per cent phenol, reduced later to 5 per cent suspension and about 0.6 per cent phenol.

The author was associated with the trials of all later methods at Kasauli.

The site for injection, etc.—The front of the abdomen is the only suitable site. The patient usually stands (he may lie down if he so desires). The needle is introduced at the prepared site (with tincture of iodine or 1 in 40 phenol) either by going into the stretched skin or at the base of a fold raised by thumb and finger. The author prefers the second method. **The needle must be of a medium bore.** Fine needles are liable to enter a venule in the adipose tissue of the abdominal wall with the result that the suspension enters the heart and distributed all over the system including the brain. The patient is likely to fall down as if shot. He recovers fairly quickly as a rule. The author has never seen this accident with a medium bore needle. Such a needle breaks the venules and therefore cannot inject into it.

The dose.—This depends on the degree of severity and the region of the body bitten, and has been lately fixed as follows :

Class I	Slight cases
Quantity for each dose 2 cc. both for children and adults. Duration of treatment 7 days.	(a) Licks, including indirect contact with saliva, on definitely remembered fresh cuts or abrasions on all parts of the body except on the head, face, neck or fingers. (b) Licks on the intact mucous membranes of the mouth, nose, anus or genitals or on the conjunctiva. (c) Bites or scratches which have raised the epidermis but have not definitely drawn blood, on all parts of the body except the head, face, neck or fingers.

Class II	Moderate cases
Quantity for each dose 5 cc. both for children and adults. Duration of treatment 14 days.	<p>(a) Licks on definitely remembered fresh cuts or abrasions on the fingers.</p> <p>(b) All bites or scratches on the fingers which are not lacerated, not more than $\frac{1}{2}$ inch long and have not penetrated the true skin.</p> <p>(c) Bites or scratches on all parts of the body except the head, face, neck or fingers which have definitely drawn blood but excluding bites which are five or more in number or in which extensive laceration has occurred.</p>
Class III	Severe cases
Quantity for each dose 5 cc. for children and 10 cc. for adults. Duration of treatment 14 days.	<p>(a) Licks on definitely fresh cuts or abrasions on the head, face, or neck.</p> <p>(b) All bites or scratches on the head, face, or neck.</p> <p>(c) Bites or scratches on the fingers which are lacerated more than $\frac{1}{2}$ inch long or have penetrated the true skin.</p> <p>(d) All bites penetrating the true skin and definitely drawing blood when these are five or more in number in all.</p> <p>(e) All bites on any part of the body causing extensive laceration.</p> <p>(f) All jackal and wolf bites.</p>

Note.—When in doubt, give a full course of treatment.

The vaccine is available from every Pasteur Institute in the Republic and from the Central Research Institute, Kasauli. It can also be borrowed in emergency from a military hospital by a medical man (and returned later).

The author recommends the maximum dose. He believes that the infection is more a matter of the maturity of the virus than of the site or severity of the wound. A mature virus may enter through insignificant breaches in the skin and kill. That is why the mortality figures vary so much in different batches: all viruses introduced by bites are not mature.

Guarding against tetanus.—This should not be forgotten when earth has been introduced into the wound. Mauling by wild animals in cultivated fields is likely to do so.

Dead virus versus live virus.—Studies (L. J. Webster, 1939, *Jour. Exp. Med.*, **70**, 87) have proved that small doses of active fixed virus do

not save animals and that the degree of immunity depends upon the quantity of the virus used. This indicates that for the treatment of human beings a dead vaccine of the Semple type in its present doses should be considered quite satisfactory: large doses of live virus would be dangerous.

Complications of the treatment.—The effect of the injection into a venule has already been noted. The only other non-specific complication occurring in some subjects is constipation due to the tenderness of the abdominal muscles consequent on a large number of injections. Ordinary complications of skin puncture (sepsis) and injection of foreign protein (urticaria, etc.) also occur.

The specific complication is the vaccine paralysis. Peripheral neuritis, myelitis and encephalitis occur. Paralysis of every kind and degree develops. Three types may be recognized: (1) Lumbo-sacral type. It is the usual type characterized by a more or less gradual paralysis of the legs and sphincters. The prognosis is good. (2) Landry type. It is characterized by sudden onset with fever, vomiting, etc., and involvement of bulbar nuclei. Death may occur. The prognosis, however, is not hopeless by any means. Recovery can occur fairly quickly. The incidence is low. (3) Neuritic type. It is characterized by involvement of peripheral nerves including the facial nerve.

Is the patient suffering from hydrophobia which the vaccine has failed to ward off, from rage laboratoire, or from complication of treatment?—The decision is very important indeed. The complication needs symptomatic treatment and chances of recovery are good. The other two are fatal. The *rage laboratoire*, of course, cannot occur with the Semple vaccine. Its existence, when vaccines containing live virus have been used, has been recognized by competent observers.

Treatment of a case of rabies.—Enough is known about protection against light and sound, and sight, sound or even mention of water. Currents of air are as disturbing (blowing on the neck will differentiate between a case of hydrophobia and lyssophobia—hysteria simulating hydrophobia, in old terminology).

It has been considered by experienced workers that if dehydration of the patient could be prevented (by rectal saline or better still glucose saline) and spasm relieved (by atropine, etc.), the disease might burn itself out. The new antispasmodic myanesin is well worth a trial. It has given promising results in tetanus (A. Das and R. C. Roy, 1949, *Indian Med. Gaz.*, **84**, 235).

The spasm is known to have passed off spontaneously. Rabbits infected with fixed virus have recovered after showing early signs of rabies.

In a state of nature (in the wild carnivores) there must be recoveries and chronic infection. The latter are definitely known in vampire bats. Biologically, it is not in the best interest of a parasite to be lethal without exception. By being so it would exhaust its nidus and become extinct. The writer advanced the view many years ago that rabies smoulders in forests and

flares in villages and towns (S. D. S. Greval, 1932, *Indian Med. Gaz.*, **68**, 451). The view has been expressed recently also (T. M. Rivers, 1948, *Viral and Rickettsial Infections of Man*. J. B. Lippincott Company, Philadelphia, London and Montreal).

(References in this series of articles are complete within the text.)

A Mirror of Hospital Practice

VAGINAL CYST

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BENIGN tumours of the vagina are rare. Of these, the cystic tumours are commoner than the solid. Cystic tumours of the vagina may have various points of origin. According to Taussig (1922), they may arise from (i) the remnants of the Wolffian duct—it being the commonest source, (ii) from an accessory ureter as a soft sac-like mass in the lateral antero vaginal wall, (iii) from epithelial inclusions produced at the time of vaginal or perineal repairs and rarely (iv) from remnants of true vaginal glands. Whitehouse (1935) cites other sources, viz, cysts of endometriomatous nature which arise in the rectovaginal septum from endometriomatous growth and project from the upper part of the posterior wall of the vagina. He records two such cases. Very rarely, there may be multilocular cystadenomata in the vagina. Occasionally also, dilated lymphatics may resemble small cysts with an endothelial lining. Again, under the influence of inflammation, cells grow down from the basal layer of vaginal stratified epithelium in the form of solid processes, from which glandular tubules may ultimately develop. From these pseudoglands small cysts arise, which may be so numerous as to be studded all over the vaginal surface. The condition in this extreme degree is very rare, and has been described by Bonney and Glendinning (Whitehouse, 1935) as adenomatosis vaginae. In fewer numbers, or as isolated examples, such cysts are not uncommon. They are usually found in the upper third of the vagina, and are generally associated with chronic inflammation of the cervix uteri.

The case recorded here is that of a cyst of Wolffian duct origin.

Case record

The patient, aged 22, para I, admitted with painless vaginal bleeding of 10 days' duration with no previous history of amenorrhœa. History of difficulty during coitus was elicited only on asking. General condition was fair. Vaginal examination revealed an anteverted, firm, regular, normal-sized uterus with normal adnexa. A sessile smooth swelling was felt high up in the vagina on its anterolateral wall on the left side. Speculum examination revealed a glistening white, thin-walled, smooth, tense cyst with a broad base, about $1\frac{1}{2}$ inches by 2 inches, projecting from the anterolateral wall on the left. There was a bad erosion on either lips of the cervix. The bleeding was uterine and fairly active. Dilatation of the cervix and curettage was done and the cyst removed.

The cyst, on puncture, produced clear, watery fluid. Its wall was thin and the inside smooth.

Histological examination revealed the following features (see figures 1 and 2, plate XLIX) : (1) The cyst wall was lined incompletely with a thin, single layer of cubical epithelium. There were a few villous projections inside the cyst cavity (A), also lined incompletely with a layer of cubical epithelium. The walls as well as the core of the villi were made of soft fibrous tissue showing some amount of degeneration in the villi (A). Situated in the wall of the cyst were seen narrow linear spaces, lined with cylindrical epithelium (B). No cilia were visible on the cylindrical cells although no special staining was done with this purpose. These spaces were evidently the remnants of the Wolffian system. Towards the vaginal side of the cyst wall were seen long narrow spaces lined with stratified epithelium, at places continuous with that lining the vagina (C) and at others, appeared to be isolated (D) completely. There were some round cell infiltration round these spaces, and also under the vaginal mucosa. The wall of the cyst also contained blood vessels and lymphatic spaces.

COMMENTS

The Müllerian and Wolffian ducts grow, during the embryonic period, in close neighbourhood. In the female, Müllerian system predominates and develops into various sex organ system. The Wolffian system atrophies and its vestiges remain in the neighbourhood of the female sex organs. The main duct called the Gärtner's duct courses in the mesosalpinx, then extends downwards along the lateral margin of the uterus (occasionally included in the uterine musculature itself) and then along the antero-lateral wall of the vagina to its lowermost portion. Usually its lumen is obliterated but often it is incomplete. Cystic dilatation of imperfectly obliterated portion of the duct may result in cyst in various portions of its course. While in the upper part of its course it may give rise to various types of broad ligament cysts, in the lower part it gives rise to vaginal cysts as is recorded here.

Character of cyst

While usually small and single, protruding into the vagina, it may be segmented and multiple and may attain a large size. When large, the cyst may burrow under the anterior vaginal wall and project inside the lumen of the vagina and even show at the vaginal introitus to simulate cystocele very closely, and it may also be associated with it. Again, it may also proceed deeply into the pelvic cellular tissue. Usually, these cysts are sessile but may be polypoid in occasional cases. The wall is thin and translucent and the content is usually watery and colourless although it may be blood-stained in some cases.

Situation

Due to the situation of the Gärtner's duct in the anterolateral wall of the vagina, the cyst arising from it also has this peculiar site. This contrasts well with the more common variety of the vaginal cyst, *viz* inclusion cysts. The latter, usually small, are situated in the lower part of the vagina in its posterior wall and only occasionally in its lateral and anterior walls. This peculiar distribution of the inclusion cysts is easily explainable by their aetiology, *i.e.* by inclusion of vaginal mucosa beneath its surface either after irregular lacerations of the vagina after childbirth or after the operation of perineorrhaphy, both by burial of mucous membrane tags when the wound is sutured.

Microscopic features

'The wall of the Gärtner's duct cysts is lined by an epithelial layer, often of undulating outline. The lining cells present many variations. Usually there is a single layer of cubical or cylindrical cells, not infrequently showing cilia. Often, however, a flattened

layer of stratified squamous epithelium is seen in part of the cyst wall. The same cyst may show different types of epithelium in different parts of its wall. When the cyst is large, the epithelium may be so flattened out by pressure atrophy as to be almost unrecognizable. In some cases, it is completely atrophied and the wall becomes denuded of its epithelial layer' (Novak, 1947). Remnants of the Wolffian system are usually visible in the neighbourhood of the cyst. In the present case, the epithelial layer consisted almost entirely of cuboidal epithelium and was denuded at places. The spaces lined with stratified epithelium and surrounded by a round cell infiltration (C and D in photomicrograph) are probably inclusions of the vaginal mucosa in its wall due to chronic infective process in the neighbourhood and are probably potentially capable of producing cyst as described by Bonney and Glendinning.

Symptoms and signs

Vaginal cysts give rise only to symptoms of mechanical origin; they may protrude at the vulva, causing discomfort and bearing down pain due to pressure on the pelvic floor muscles. They may occasionally cause difficulty in coitus. In the present case, the cyst was moderate in size and produced slight dyspareunia as the only symptom.

Treatment

When small and symptomless the cyst does not require any treatment but when there is symptom it should be treated with surgical excision.

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ERRATUM

THE PRESENT STATUS OF SULPHONES IN THE TREATMENT OF LEPROSY

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In the above article published in the *I.M.G.*, 85, No. 8, August 1950, p. 348, in the chart, the link between the second and third lines in the formula of the 4th group, *i.e.* sulphetrone and novetrone, should be removed.



Fig. 1.

A=A villus projecting into the cyst cavity and lined by cuboidal cells and showing some degeneration.
B=Remnants of Wolffian system, a linear, narrow space lined by cylindrical epithelium.



Fig. 2.

C=Linear space lined by stratified epithelium and continuous with that lining the vaginal mucosa.
D=Narrow space lined by stratified epithelium appearing to be completely isolated from vaginal epithelium (E).

Indian Medical Gazette

OCTOBER

RABIES

THIS virus encephalitis not being a public health problem has never interested very deeply the medical profession generally. Our reasons for taking notice of it are : (1) Lately, during the last three years or so, sporadic cases of acute virus diseases of the central nervous system have shown a definite increase all over the country. They are likely to cause confusion clinically, as all forms of virus encephalitis must have some clinical features in common. (2) Carnivores of the jungle have turned their attention to human habitation and are attacking women, children and domestic livestock, specially in the U.P. (Daily Press, 1950). This is obviously a result of reclamation of fallow land in the 'grow more food' campaign, and the events in the U.P. have attracted more attention because of the greater number of towns and villages in this State. As has been suggested during the last two decades, the disease probably comes into human habitations from the wilderness (Greval, 1932; Rivers, 1948). It is likely to increase with the increase in the growth of food. The wild carnivores dislodged from their wild haunts will continue coming villagewards and townwards, until their numbers are decreased by shikaris and by unfavourable environment for reproduction. While all warm-blooded animals are affected, the carnivores from the tiger (Pandit, 1950) to the mongoose (Greval, *loc. cit.*) are specially susceptible. Those attacking dogs are particularly dangerous. Incidentally, foxes, unlike jackals, do not turn on the dogs in a hunt. (3) In this issue appear no less than five communications on rabies. This is an exceptional event.

A brief history of antirabies prophylaxis, after a bite, in India.—(1) In 1900 was started at Kasauli The Pasteur Institute of India, with Major Semple of the R.A.M.C. (later Sir David) as its first Director. This worker had studied the various forms of treatment given in Paris, Vienna, Budapest and Rome, and had come to the conclusion that the fixed virus of rabies (in the spinal cord) killed with phenol and diluted to contain 1 per cent of nerve tissue with 0.5 per cent of phenol was as good as any other type of vaccine. Further, it was entirely free from the risk of laboratory rabies arising from the use of live virus. This was the Semple vaccine (for further details see p. 453). (2) In 1926-1930 were tried at Kasauli 'ether vaccines'. They were made from rabbit brains

containing fixed virus, immersed in ether (Cunningham, Nicholas and Lahiri, 1926). A serious flaw in these vaccines was that they were used fresh and no previous sterility tests were possible. They reduced the mortality. (3) In 1932 it was considered that a 5 per cent Semple vaccine could be equally effective and definitely safer inasmuch as it could conform to the bacteriological etiquette of a test for sterility. This vaccine is now in use all over India. Strange though it may seem one Province (now State) carried on with the old 1 per cent vaccine for many years before falling in step with the rest of the country. (4) The increase in the strength of the nerve tissue made it necessary to culture the fixed virus in an animal larger than the rabbit. Sheep had already been found suitable (Editorial, 1930). The present 5 per cent Semple vaccine is made from sheep brain. (5) A virus culture as a vaccine is still under trial. (6) Administration of antirabic serum has been thought of and tried from time to time. Its use in serious bites (on head and hands, see p. 454 for classification of the bites) is a rational therapeutic measure.

(The Pasteur Institute of India, Kasauli, remained the only Centre for treatment of and research on rabies for many years. In 1912 it treated 3,458 patients and thus became the largest institute in the world—Current Topics, 1913, The Prevention of Rabies.)

The Pasteur Institute of Southern India, Coonoor, was opened in 1907. It started functioning next year.

At a later period were opened other Pasteur Institutes and Centres for antirabic treatment to complete decentralization. In 1939 The Pasteur Institute of India, Kasauli, was closed and the making of antirabic vaccine, etc., was taken over by The Central Research Institute, Kasauli.

Efficacy of the treatment.—From Pasteur's time mathematical obfuscation has not been lacking to 'show' that the prophylaxis of rabies was of little or no use. 'Considerations such as these have led many workers to question the value of the vaccine treatment of rabies' (Wilson and Miles, 1946). Two observed facts only are sufficient to refute the obfuscation : (1) In the same institution, during the same period, dealing with the same classes of bites, mortality fell almost to half when the strength of the vaccine was increased. This occurred at Kasauli in 1932. (2) The mortality figures of the Province (now State) which carried on with 1 per cent vaccine for many years were higher than those elsewhere (hence the change-over to the stronger vaccine ultimately). On the efficacy of the treatment there should exist no doubt whatsoever.

(The Semple vaccine in the U.S.A. is an antirabic vaccine prepared from 4 per cent inoculated rabbit brain treated with 0.5 per cent

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Medical News

PRESS NOTE

(Issued on 29th September, 1950, by Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta)

THE Government of India have deputed Dr. A. R. Mehta of the Directorate-General of Health Services to pay a flying visit to Jammu for discussions with the Chief Medical Officer there with a view to deciding what medical relief measures are necessary on account of the damage caused by recent heavy floods. Dr. Mehta left Delhi by air for Jammu on 26th September, 1950.

MAN'S EXPECTATION OF LIFE 'CONSIDERABLY INCREASED'

B.M.A. PRESIDENT'S DISCLOSURE

(From Release No. B.F. 929 issued by British Information Services, New Delhi)

DURING the past 50 years man's expectation of life has considerably increased. This is revealed by the President of the British Medical Association, Sir Henry Cohen.

Sir Henry says that there have been considerable changes in the pattern of life. 'Since the start of the century the expectation of life at birth has increased for the male by 18½ years and for the female by over 20 years. A man of 40 to-day can expect to live another 31 years and a woman another 35.

'There have also been changes in the pattern of medical treatment. Improvements in radiology enable us to visualize practically every crevice and cavity of the body. It has advanced the accuracy of diagnosis to an almost incredible degree. The radio-active isotopes now being produced at the British Atomic Energy Establishment promise yet further advancement.'



NEW SUPER X-RAY MACHINES FOR CANCER TREATMENT

Resources under the National Health Service for the treatment of cancer and other diseases will be considerably strengthened when five super-voltage x-ray therapy machines of new design become available for use in the United Kingdom. The machines, of all British design craftsmanship and materials, will be capable of producing the effect of four million volt x-rays. They are known as Linear Accelerators. This sketch is the Metropolitan-Vickers conception of what one of the Linear Accelerators will look like.

The following 3 items are reproduced from Press Releases issued by W.H.O. Regional Office for South-East Asia, New Delhi :—

(1) W.H.O. ANTI-MALARIA PROJECT IN REMOTE AREA OF NORTH AFGHANISTAN

TEAM LED BY INDIAN EXPERTS

(SÊA/PR/50-39, dated 18th August, 1950)

A W.H.O. malaria control project recently launched in North Afghanistan is operating in 'one of the wildest and most remote regions it is possible to imagine', according to Dr. S. L. Dhir, Malariologist to the W.H.O. team, who this week returned to Delhi for a few days. Dr. Dhir has now left again to rejoin the team in the Kundus-Khanabad area of Kataghan Province, 25 miles from the permanently-closed border

of Russian Turkestan, and 310 miles from Kabul by what Dr. Dhir describes as 'perhaps one of the roughest roads in the world'.

The W.H.O. malaria team in Afghanistan is led by Mr. T. Ramachandra Rao, of the Bombay State Malaria Organization, who last year made a rapid survey of the Kundus-Khanabad area for W.H.O. In May 1950, Dr. Dhir, who belongs normally to the Delhi Malaria Institute, accompanied Mr. Rao to Kabul where they loaded their jeeps and trucks with the supplies and equipment which were waiting for them there, and set out on the three-day road journey north. At their headquarters in Kundus they have since been joined by Mr. J. N. Mitroo, also of the Delhi Malaria Institute and Mr. J. Lanoix, W.H.O. Sanitary Engineer from island of Haiti. Twelve other team members have now been assigned to the project by the Afghan Government.

In spite of the difficulties of supply and communication, and the time needed to train DDT spraying squads, insect collectors and microscopists, Dr. Dhir reports that it has already been possible for the team to carry out spleen surveys and to take blood slides from children in more than 25 villages, and to launch DDT spraying operations in a large part of the area.

According to Dr. Dhir, at first the village people are naturally suspicious of strangers. Fortunately however the local police officials are co-operating whole-heartedly and accompany the team-members in their first visits to each village. 'If we went alone', states Dr. Dhir, 'we should not have access to any houses nor be able to carry out the survey work essential to enable us to assess the amount of malaria existing before our spraying operations begin'. In one village Dr. Dhir found that nothing could be done until the local maliks and village elders could be convinced that the government was not going to levy a new tax on villages which had been sprayed by the team.

In the first year of operations the team plans to control malaria in a 200 sq. mile area centred around Kundus and Khanabad in the valley of the Talaqan, a tributary of the famous river Oxus. Although surrounded on all sides by desert, the valley is very fertile. Unhappily much of it is also, according to Dr. Dhir, a hyperendemic malarious area. Malaria control may therefore be expected to exert an important influence on the progress of agricultural and economic development in the area.

The Khanabad-Kundus malaria-project is the seventh to be launched in S.-E. Asia with active, practical co-operation from W.H.O. Of the others, four operate in India and one in Thailand, while the sixth which terminated last year was in the Laghman district of Afghanistan.

(2) FIRST DEPUTY DIRECTOR-GENERAL OF W.H.O. APPOINTED

(SEA/PR/50-40, dated 18th August, 1950)

A CABLE from W.H.O. Geneva Headquarters, dated 17th August, announces the appointment of Dr. Pierre Dorolle (France) to the newly-created post of Deputy Director-General of the World Health Organization. Dr. Dorolle was formerly Director of Health Services in Indo-China.

Born in 1899, Dr. Dorolle studied in Paris and Bordeaux (France), specializing in Tropical Medicine. In 1925 he began service in Indo-China. His wide experience which included the control of epidemics of plague, smallpox, cholera, typhus, and diphtheria led to his appointment to the League of Nations Epidemics Commission in China in 1937.

Recalled to Indo-China in 1940, Dr. Dorolle was subsequently interned by the Japanese. After the liberation, he was responsible for reorganizing the health services of the country, and for arranging their

transfer to the new States of Viet Nam, Cambodia and Laos.

Dr. Dorolle was a member of numerous Far Eastern Health Missions, and is the author of several publications on Tropical Pathology, Tropical Hygiene and Nutrition. He holds the Croix de Guerre for Resistance activities, and is Member of the Legion d'Honneur.

Until Mr. Dorolle's appointment, Dr. Brock Chisholm (Canada), W.H.O. Director-General, had no Deputy. Earlier in the year both the W.H.O. Executive Board and the World Health Assembly had emphasized the importance of filling the new post.

(3) DELHI TRAINING CENTRE FOR CHILDREN'S DOCTORS AND NURSES PLANNED

(SEA/PR/50-42, dated 25th August, 1950)

A W.H.O. TEAM composed of a paediatric specialist and a paediatric nurse is at present attached to the staff of the Irwin Hospital, New Delhi. They are giving practical help to the hospital in planning the development of its facilities for the treatment of sick children. This is part of W.H.O.'s contribution to a large-scale joint project of the National Health Service and UNICEF aiming at developing in Delhi a modern training centre in both theoretical and practical aspects of child care and the treatment of children's diseases.

The United Nations International Children's Emergency Fund (UNICEF) has allocated a sum of \$253,000 towards the project which will train paediatricians and paediatric nurses from all over India. The money will be used to provide personnel and equipment both for the Maternal and Child Health Project already taking shape in a rural area of Delhi Province, and for upgrading the children's wards in a number of Delhi hospitals. W.H.O. is providing expert technical guidance for the whole project.

Plans are also being finalized for building at Government expense a new and up-to-date children's ward at the Irwin Hospital.

The two members of the W.H.O. team are Dr. B. Landtman (Finland) and Miss Nancy Toy (Canada). Dr. Landtman is a paediatric expert who has worked in the Children's Hospital of the University of Helsinki (Finland) and subsequently in children's hospitals in London and Stockholm (Sweden). Miss Toy has done teaching work in the Toronto Hospital for Sick Children, and was on the staff of the Montreal Child Health Association in Canada. In addition to her work at the Irwin Hospital, she is at present giving instruction in paediatric nursing to students of the Delhi College of Nursing.

The following 6 items are reproduced from Releases issued by Pan-American Sanitary Bureau Regional Office, World Health Organization, 2001, Connecticut Avenue, N.W., Washington 8, D.C. :—

(1) MALARIA RATE REDUCED IN AREA OF PAKISTAN SPRAYED IN PROJECT OF W.H.O. AND U.N. CHILDREN'S FUND

(Geneva, 15th August)

A STRIKING reduction in the rate of malaria among the rural population of the Mymensingh District of East Pakistan has been reported by Dr. Gabriele Gramiccia, leader of the World Health Organization's Malaria Control Team which for the past year has carried out a DDT spraying project.

Dr. Gramiccia's report, received in Geneva, shows that not a single case of new infection has been found among persons living in the area covered since spraying operations began. Enlarged spleen, a typical malaria manifestation, has been reduced among children of the area from 75 per cent to 21 per cent.

Meanwhile, in the surrounding unsprayed areas, numerous new cases of malaria have been reported.

Anti-malaria protection was provided by the team to about 35,000 people in 1949. More than 22,500 rooms were sprayed. This year the team undertook to protect a much wider area, including about 250,000 people living in more than 40,000 houses.

The total cost of protection per person amounted to about one-third of a day's wage for the average rural labourer in the district. Since it is estimated that the labourer loses about 15 working days annually because of malaria, the worker's financial loss from malaria would be 45 times greater than the cost of being protected.

The encouraging results, Dr. Gramiccia stated, had a profound effect on the population, which at the beginning had taken a rather diffident attitude. The people are now not only appreciative but earnestly request continuation of spraying and extension of the programme to neighbouring regions.

At the same time, the team reported results of a survey of kala-azar (a disease transmitted by the sand-fly and second only to malaria in its incidence throughout large parts of Asia). Five thousand children in the area have been tested, and more than 10 per cent found infected.

The four-member team has also been carrying on public health work in villages, with emphasis on the teaching of elementary hygiene and maternal and child health practices.

The project has been carried out jointly with the United Nations International Children's Emergency Fund, which provides supplies and equipment. Each team member has one or more understudies so that, after completion of the present project, the work can be continued by local authorities.

(2) POLAND ANNOUNCES DECISION TO WITHDRAW FROM WORLD HEALTH ORGANIZATION

(Geneva, 15th August)

THE following communication was received to-day, by Dr. Brock Chisholm, Director-General of the World Health Organization, from Junian Przybos, Minister of Poland at Berne, Switzerland:

'By order of the government of the Republic of Poland, I have the honour to bring to the attention of the World Health Organization the following:

'Poland gave adhesion to the World Health Organization in firm belief that the Constitution provided the basis for action toward eliminating the effects of war, raising health levels of all peoples of the world and helping to fight for lasting peace and against aggressive warfare, the cause and source of disease and human suffering.

'Unfortunately it became apparent already at the first plenary session of W.H.O. that one state, the United States, demanded a special status within the organization, especially regards the budget. The Polish delegation drew attention to manifest violation of statutory dispositions of W.H.O. But the United States continually opposed decisions of the World Health Organization, violated decision, submitted W.H.O. to its own political ends.

'Thus during its Third Session at Geneva, the Executive Board learned and approved of the action of the Director-General in attempting to arrange for export six Podbielniak extractors from the United

States into certain European countries, among them Poland, in order to increase production of penicillin, a substance of capital importance for health. However, the United States refused to carry out the recommendation of the Executive Board. In the same manner, it rendered impossible exchange of information on antibiotics research concerning such products as streptomycin, aureomycin, etc., thus prejudicing the W.H.O. basic principle that each country may participate in the results obtained anywhere in the field of health protection. At the same time the government of Poland must also state that W.H.O., despite the decision previously taken by the Director-General, subsequently endorsed by the Executive Board, allowed the attitude of the United States, an attitude contrary to elementary humanitarian principles, to go unchallenged.

'The fact that W.H.O. did not make objection when the committee of experts on health matters was formed within the framework of the western union, an organization obviously aggressive in character, further shows how W.H.O. gave in to American pressure, how it shifted to political positions contrary to the concept of peace. This happened in spite of protests raised by several delegations which during the Second World Health Assembly had revealed the contradiction existing between that attitude and the principles expressed in Articles 44 and 45 of the Constitution of W.H.O. Furthermore, W.H.O. never raised its voice against criminal plans for using atomic and bacteriological weapons.

'Lastly, W.H.O. lately gave further proof of lack of faith in the principles which should guide its work, as well as complete surrender to imperialistic states, particularly the United States, in admitting as members the unrepresentative cliques of Bao Dai and Li Syn Man (Syngman Rhee) and inviting the Kuomintang clique to the Third World Health Assembly.

'Polish delegations repeatedly protested during sessions of the Health Assembly and Executive Board against submission of W.H.O. to such a policy. At the same time Polish delegations made suggestions designed to maintain the true character of W.H.O. by strict observance and execution of its Constitution. These suggestions were systematically rejected.

'Taking the facts into consideration, the government of the Republic of Poland declines to take responsibility for the orientation of activities of W.H.O. and for submission to the imperialistic policy of powers preparing for a new war, and signifies by the present letter its decision to withdraw from W.H.O.

'At the same time the government of the Republic of Poland expresses its willingness to co-operate in the field of Health with all nations devoted to peace and opposed to wars of aggression.'

(3) W.H.O. EXPERT GROUP DEFINES PRINCIPLES OF HEALTH CARE NEEDED BY SCHOOL-AGE CHILDREN

(Geneva, 16th August)

BASIC principles for provision of health care for school-age children have been defined for the first time on a world-wide basis by a group of medical officers, paediatricians, school physicians, health educators and nurses called together by the World Health Organization, W.H.O. announced to-day in Geneva.

The expert committee on school health services, which met at Geneva from 5th to 12th August, emphasized the need for school services to be organized as 'team projects' involving parents, the community, professional groups, social agencies and others interested in child welfare. Moreover, the committee pointed out, school health services should be a direct continuation of pre-school services.

The expert committee stressed the belief that schools in all areas, particularly in underdeveloped regions,

should serve as demonstration centres for public health measures. Sanitary school buildings not only should promote the child's health but also should serve as an educational example for the community, it was stated.

The committee listed minimum comprehensive, continuous functions to be performed by school health services:—

1. Medical supervision and dental hygiene.
2. Communicable disease control. Preventive measures against communicable childhood diseases should be organized by each school.
3. Nutrition. The committee believed that schools, particularly in areas of low economic status, have an important function in actual provision of meals, and that nutrition education should go along with meals.
4. Mental health. Since schools provide an excellent opportunity for detection of psychological problems in children at an early stage the committee stressed the value of mental health programmes in schools and emphasized the rôle of the school-teacher.
5. Health education. The committee recommended establishment, wherever possible, of health education programmes in co-operation with parents and community groups.

The experts also stressed the need for organization in all schools of school-teams composed of doctor, nurse and teacher. Health work should be planned jointly and carried out co-operatively by teachers, physicians, nurses, other specialists and administrators, it was said.

The meeting was attended by Jacob H. de Haas (Netherlands), Dr. Myron E. Wedman (U.S.), Dr. Emmanuel C. de Castro (Brazil), Miss Hanna Liadquist (Sweden) and Dr. Dorothy B. Nywander (U.S.) and Dr. Fraser C. Brockington (U.K.).

(4) W.H.O.-UNICEF EXPERTS TO AID IN YAWS-CONTROL CAMPAIGN IN THAILAND

(Geneva, 17th August)

Dr. DONALD R. HUGGINS, an expert consultant of the World Health Organization and the United Nations International Children's Emergency Fund, has gone to Thailand to assist in a training and demonstration programme for the control of yaws, planned as the springboard for expanding existing yaws-control services into a nation-wide campaign.

Dr. Huggins, formerly in charge of yaws and venereal disease control in Trinidad, British West Indies, recently conferred in New Delhi with W.H.O. and UNICEF officials regarding plans for the training project. UNICEF has allocated \$92,000 to provide necessary supplies and international personnel for Thailand's anti-yaws campaign.

Yaws, a disease resembling syphilis but non-venereally transmitted, is reported to affect at least 200,000 people in all parts of Thailand. It is estimated that four-fifths of those suffering from the infective stages of the disease are persons under 18 years and women of child-bearing age.

The Thai anti-yaws training project will operate in Ratchaburi Province under the direction of Dr. Boon Suramasara, director of the venereal disease control division of the Thai Public Health Service, who last year spent six months in the United States as a W.H.O. Fellow studying latest advances in the diagnosis and treatment of venereal infections. He will be assisted by two Thai doctors who recently completed training at the Simla headquarters of a W.H.O. venereal disease control team now working in the Himachal Pradesh district of Northern India.

Dr. Huggins' assignment will be to aid the Thai health authorities in organization and day-to-day

operations of the training programme in the field. He will be assisted by Dr. K. Urdal of the Oslo Bacteriological Institute of Norway, a W.H.O.-UNICEF laboratory expert, and probably a W.H.O.-UNICEF Public Health nurse. Dr. Urdal, now at Simla with the W.H.O. venereal disease team, will go to Thailand shortly.

The main function of the Ratchaburi yaws-control demonstration project, Dr. Huggins has explained, will be to train teams of Thai health workers who will later extend the anti-yaws campaign into all parts of the country. The teams will work by systematic house-to-house visits to discover all existing cases and to ensure their receiving penicillin treatment.

(5) W.H.O. TO SEND HEALTH OFFICERS TO KOREA TO AID IN RELIEF PROGRAMMES FOR CIVILIANS

(Geneva, 19th September)

The World Health Organization has announced in Geneva plans for sending specially selected officers to Korea to assist in the administration of health and relief programmes for the civilian population.

The Senior Officer is Colonel Walter H. Crichton, who was scheduled to leave Geneva to-day and travel to his new post by way of New York.

In addition, five public health teams composed of medical officers and sanitary engineers, now being recruited by W.H.O. in Europe, South America and the United States, will be working among Korean refugees. Colonel Crichton and two other officers will be available to assist the Korean Ministries of Public Health and Social Welfare and will help reorganize health services, assist in relief programmes, and aid in the control and prevention of epidemics.

Dr. Crichton, whose home is in Eastling, Faversham, Kent, England, joined the Indian Medical Service and later served in Iraq and Italy. He was Director of Public Health and Welfare with the 21st Army Group in Western Europe.

(6) CARIBBEAN RABIES CONFERENCE RECOMMENDS CO-ORDINATION OF RABIES CONTROL IN AREA

(Washington, 25th September)

FOLLOWING a 3-day review and discussion of the rabies situation in the Caribbean area, at a Rabies Conference held in Kingston, Jamaica, 28th to 30th August, 1950, several important recommendations were presented to the governments of the islands, outlining measures for effective rabies control and strongly urging their application by health authorities.

The Caribbean Rabies Conference, representing the first attempt toward co-ordination in the area of anti-rabies measures heretofore limited to certain islands, was organized by the Pan-American Sanitary Bureau, Regional Office of the World Health Organization. Its purpose was to review the rabies situation in the area and study control measures now in effect; to exchange information on the latest techniques of diagnosis, control and eradication of rabies; and to make recommendations for concerted anti-rabies measures among the governments in the Caribbean area.

Upon his return to Washington, Dr. Benjamin D. Blood, Chief of the Veterinary Public Health Section of the Pan-American Sanitary Bureau, declared: 'The Rabies Conference was an outstanding success and the forerunner of a well-integrated programme for the control of rabies in the Caribbean area.'

The island governments were represented by health officials who participated in the Conference's informal sessions held under the chairmanship of Dr. S. E. Ferreña, Acting Director of Medical Services of Jamaica. Other delegates were: Sr. José de Jesús

military and civilian hospitals. The Red Cross Society took over the staffs previously supplied by the Army; the State Governments undertook to help the respective branches financially.

Since this service was set up nearly 10 years ago, more than 680,000 Australians have donated 595,000 pints of blood. In 1949, 85,000 people gave 74,873 pints. Hundreds of lives have been saved.

A typical branch of the service is that in Sydney. This is also the largest and costs Rs. 4,00,000 a year to run. In 1949, the Sydney branch took blood from 40,000 donors. Thirty-three per cent of this blood was converted into serum. In the first quarter of 1950 it sent out more than 7,000 pints of blood given by 8,000 volunteers.

A 24-hour blood service is provided by a staff of 80, which includes three doctors, five nursing sisters, two science graduates and nurses and laboratory assistants. They collect blood from about 150 donors a day, and after testing it, distribute it to hospitals in Sydney and throughout the State.

The Service has never failed to answer an urgent appeal. There have been many life-and-death dashes with serum and whole blood, both to city clinics and to bush hospitals hundreds of miles away.

Blood service cars, equipped with sirens, have the right-of-way in city traffic, when carrying blood on serious calls. Cars and planes are used for distant deliveries.

The Sydney branch provides every hospital in New South Wales with a supply of serum for emergencies. (In country localities, whole blood is usually supplied on a direct donor-to-patient basis by a panel of approved donors.)

Since the Sydney branch began in 1941 it has taken blood from nearly 400,000 people. Approximately 21,600 of these donated whole blood to the armed forces; 125,900 donated whole blood to civilians. In the same period, blood from 121,000 donors was made

into serum for the forces, and the blood from 82,900 people into serum for civilians.

Many donors give a pint periodically. A member of the New South Wales Legislative Council, Mr. A. P. Bridges, has given the largest number of donations to date—39. Others have given nearly as much. Blood is never taken from a donor more than once in three months.

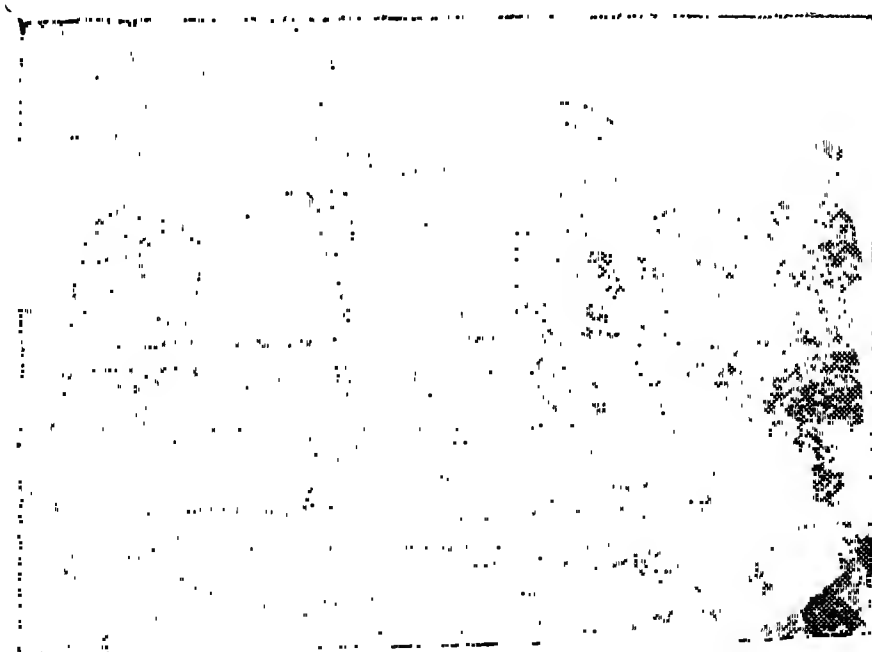
Blood is taken only from medically-certified donors between the ages of 18 and 60. Sixty per cent are women.

Procedure in blood taking is similar to that practiced elsewhere. A donor visits the New South Wales Transfusion service at its headquarters in George Street, Sydney. A careful check is made to ensure that he can spare the blood. His finger is pricked and a sample of his blood taken. Assistants then determine from his blood count and weight how much he can safely give.

In 15 minutes, 500 cubic centimetres (nearly a pint) of his blood flows into a bottle kept just out of his line of vision. After a half hour rest, the donor is free to leave. His blood has been mixed up meanwhile with an anti-coagulant to check clotting and it is then subjected to ultra-violet rays to kill possible bacteria.

The bottle top is then dipped in a plastic sealing solution, a small bottle containing a specimen of the donor's blood is wired on and the donation is ready to be stored or sent out.

The service likes to keep a generous stock of group O (universal) blood, which 47 per cent of Australians have and which can be given in an emergency to patients of the other groups A, B and AB. The service hopes shortly to be able to provide fractionized serum—serum which has been broken up into its various components, each one of which is valuable in a particular disease. This project is being paid for by the Federal Government, which has made available its Serum Laboratories in Melbourne, Victoria.



THE QUEEN VISITS NOTTINGHAMSHIRE

During a two-day visit to Nottinghamshire, H.M. the Queen opened the Portland Training College for the disabled at Mansfield. The College which is the first of its kind in the Midlands will serve the counties of Nottingham, Lincoln, Derby, Leicester and Rutland, and is already being used for the rehabilitation of injured patients. The Queen later also paid a visit to the Harlow Wood Orthopaedic Hospital near Mansfield, where she is seen watching a patient being lowered into the Remedial Swimming Pool on a special apparatus.



ELECTRICALLY CONTROLLED PAGE-TURNER

A patient in an 'iron lung' in a hospital in Britain reading a book by the aid of a machine. The machine is electrically controlled and the slightest pressure on a button on a panel by the patient's chin will turn the pages as required.

BRITISH JOURNAL OF TUBERCULOSIS AND DISEASES OF THE CHEST

Dr. PHILIP ELLMAN is succeeding Dr. Clifford Hoyle in the editorship of the *British Journal of Tuberculosis and Diseases of the Chest*, after the publication of the July issue, and he will be assisted by an Editorial Board which, in addition to Dr. Clifford Hoyle, comprises Mr. T. Holmes Sellors (London), Dr. A. Brian Taylor (Birmingham) and Professor Cameron (Edinburgh).

Dr. Clifford Hoyle succeeded the late Dr. L. S. T. Burrell in 1938 and has, therefore, edited the journal for twelve years.

INDIAN PHARMACEUTICAL CONGRESS

THE Third Session of the Indian Pharmaceutical Congress will be held at Calcutta on the 30th and 31st December, 1950. The Executive Committee are trying to organize it on a very broad scale and

scientists of repute from different parts of Asia as well as from U.K., U.S.A. and other countries are expected to attend the session. An important item of the programme will be to read and discuss scientific and research papers on various aspects of Pharmacy and allied subjects.

President Elect :

Dr. Sir J. C. Ghosh, *Kt.*, D.Sc., F.N.I., F.R.A.S.B.

President :

Dr. K. A. Hamied, J.P., B.Sc., M.A., Ph.D. (Berlin), F.R.I.C., F.C.S. (Lond.), M.L.C.

Sectional Presidents :

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Sister Jane Francis, B.Sc. (Pharm.), Holy Family Hospital (Patna).

Section of Pharmaceutical Chemistry

Dr. D. L. Shrivastava, D.Sc., Assistant Director (Planning), Central Drugs Research Laboratories (Lucknow).

Section of Pharmacognosy

Dr. K. P. Biswas, M.A., D.Sc. (Edin.), F.R.S.E., F.N.I., F.B.S., Superintendent, Indian Botanic Garden (Howrah).

Section of Pharmacology

Professor Dr. B. N. Ghosh, M.B.E., F.R.F.P.S. (Glas.), L.M. (Dub.), F.S.M.F. (Beng.), F.R.S. (Edin.), Professor of Pharmacology, R. G. Kar Medical College (Cal.).

Section of Ayurvedic Medicine

Vishak Shiromani Panditbhusan Kaviraj Bimalananda Tarkatirtha, Byakarantirtha, Shastri, Saraswati.

Chairman of the Reception Committee :

Dr. S. B. Dutt, M.A., Ph.D. (Lond.), Sheriff of Calcutta.

Enquiries to :—

Dr. P. K. Sanyal, Ph.D. (Lond.), Ph.C. (General Secretary).

FACILITIES FOR POST-GRADUATE MEDICAL STUDIES

(From a Note dated 26th August, 1950, issued by Press Information Bureau, Ministry of Information and Broadcasting, Government of India, Calcutta)

THE Vienna Academy of Medicine has offered facilities for post-graduate work in the following medical subjects :—

1. Ophthalmology.
2. Pathology.
3. Pharmacology.
4. Surgery.
5. Gynaecology.
6. Internal Medicine.
7. Ear, Nose and Throat.

Medical graduates, desirous of undergoing training at their own expense, may apply to the Under-Secretary to the Government of India, Ministry of Health, New Delhi, with full particulars of their qualifications, age, present position, experience, etc., not later than 10th September, 1950.

The courses start in October 1950 and range from one to two years. The total charges for the classes as well as boarding and lodging will not exceed those now incurred in connection with similar courses of studies in the United Kingdom.

NUFFIELD FOUNDATION TRAVELLING FELLOWSHIPS AWARDS TO INDIAN GRADUATES

THE Nuffield Foundation, with the object of advancing the interests of India as a whole and further strengthening the academic ties between India and the United Kingdom, has decided to make available to India five Travelling Fellowships for the year from 1951-52. An Advisory Committee in India has been appointed by the Foundation to advise them on the administration of the scheme, consisting of Shri Gaganvihari L. Mehta, Member, Planning Commission (Chairman), Shri S. Varadachariar, Dr. C. V. Raman and Shri J. J. Ghandy. It has been decided to award the Fellowships for the year 1951-52 in the following subjects :—

Two Fellowships in Medical Sciences, preference being given to candidates wishing to study : (1) Physiology or Bacteriology, and (2) Industrial Medicine or Public Health,

One Fellowship in Engineering, preference being given to candidates wishing to study Electrical Engineering (Generation or Distribution),

One Fellowship in Natural Sciences, preference being given to candidates wishing to study Plant Genetics or Soil Science, and

One Fellowship in Social Sciences, preference being given to candidates wishing to study Industrial Relations or Personnel Management, and Agricultural Economics.

The purpose of the Fellowships is to enable Indian graduates of outstanding ability to gain experience and training in the United Kingdom in their chosen fields, and to make contact with scholars working in those fields, with a view to the Fellows equipping themselves to take up senior posts in research and teaching in India.

The Fellowships are intended for men or women of first-rate intellectual and personal qualities, who have already shown unusual capacity to advance knowledge and teaching in one of the fields concerned. Candidates must be Indian nationals, normally between the ages of 25 and 40 years, and must be university graduates holding, preferably, a Master's or Doctor's degree, and having subsequently had a year or more of teaching or research experience on the staff of a university or comparable institution.

A Fellowship will normally be tenable for one year, but in exceptional cases may be extended for a further period of a few months by the Trustees and after consultation with the Foundation's Advisory Committee in India. Its value will be adjusted to suit the needs of the holder. It will be made on the basis that the Foundation provides the Fellow with free board and residence, and meets approved travelling expenses to, from and within the United Kingdom, and approved research or like fees. The only payment made direct to a Fellow will be an allowance to cover other personal expenses. It is estimated that the total value of an award (exclusive of travelling expenses) will be at the rate of from £770 to £890 a year (sterling), according to individual circumstances.

In addition, the Foundation will pay the travelling expenses to and from the United Kingdom of a Fellow's wife, if he is married at the time he makes his application, in those cases in which the Advisory Committee agrees to a Fellow being accompanied by his wife.

A Fellow will be expected to resume residence in India on the completion of the Fellowship.

Except with the express permission of the Trustees of the Foundation, a Fellow may not hold any other award concurrently with the Fellowship.

A Fellow will be required to carry out, at centres approved by the Trustees of the Foundation, a programme of research work and training similarly approved. Other work, paid or unpaid, may not be undertaken without the permission of the Trustees. During the tenure of the Fellowship a Fellow will not be permitted to prepare specifically for, or to take, examinations for higher degrees or diplomas awarded by bodies in the United Kingdom.

A Fellow will be required to submit to the Trustees, at the end of the Fellowship, a report on his work during the Fellowship.

Should the Trustees at any time find that a Fellow neglects or has neglected the obligations of the appointment, they shall have power immediately to terminate the Fellowship.

The Fellowships will be awarded by the Trustees of the Foundation on the recommendation of its Advisory Committee in India.

Applications for Fellowships to begin in 1951 should be submitted not later than the 31st March,* 1951, to the Secretary, Nuffield Foundation Indian Advisory Committee, c/o Planning Commission, Government House, New Delhi, from whom copies of the form of application may be obtained.

(Sd.) L. FARRER-BROWN,
Secretary, Nuffield Foundation.

* Changed to 28th February later.

Public Health Section

A 'NEW LATRINE' SUITABLE FOR RURAL COMMUNITIES, CAMPS AND ISOLATED BUNGALOWS

By R. B. LAL, F.N.I.

Department of Epidemiology, All-India Institute of Hygiene and Public Health, Calcutta

PROBLEMS confronting the rural populations are many and varied. Of these problems, environmental sanitation is one of the most pressing and perplexing ones. To be a real success the solution of this problem must be effective and practicable. A method must be devised, which will be simple, that is to say, it will cause little or no interference with the rural environment, with the prevalent cultural values, with the social practices and even prejudices and with personal comforts; which will be economically sound, that is to say, it will not cause wastage of manurial value of putrescible organic matter and will be well within the reach of the poverty-stricken rural population; and which will be entirely satisfactory from the health point of view and will cause no nuisance from smell or fly breeding. The method must be fool-proof in operation and, if possible, the equipment involved in it should be capable of being manufactured by local artisans with locally available material.

So far as night-soil is concerned, any method involving its collection, removal and disposal must obviously be ruled out. The nearest approach which has so far been made towards the solution of this problem is the borehole latrine.

In a group of 90 villages in West Bengal, such latrines have been installed over a number of years. The boring has been done under the supervision of a government agency, to a depth of 15 feet or so reaching 3 feet below the subsoil water-level, making a charge of Rs. 2 for labour. The same agency has prepared and distributed at cost price (Rs. 3 each) cement-concrete squatting plates measuring $2\frac{1}{2}$ feet by 3 feet. These plates have been placed over the openings of the bored holes. They have been moulded into a suitable shape so as to provide foot-rests and to drain away urine and ablation water towards the central hole through which the faeces directly drop into the bored hole. It has been generally found necessary to prevent caving of the walls of the bored holes by such devices as 'split bamboo-jafree' or with 'baked clay rings' with multiple holes, the cost in either case being Rs. 4 per latrine. The clay rings which have so far been made to order for experimental purposes should cost much less, perhaps Re. 1 per pair, if they come into general use. They will have further advantage over the bamboo-jafree in that they

will not rot and fall reducing the capacity of the hole. The villagers are asked to provide the superstructure for protection from rain and sun and for privacy, employing bamboo frames, bamboo-jafree and other locally available material.

This device has not succeeded in catching the imagination of many people and some of those who had a bored hole latrine installed in the house have abandoned its use because of the following difficulties:

(1) Not being accustomed to confined places, people do not get satisfactory evacuation and prefer to sit in the open or behind bushes for privacy, if necessary.

(2) The plate is frequently soiled by improper use and becomes unfit for the next person unless properly cleansed, and few people will take the trouble to do so.

(3) The bored hole rapidly fills up and a new hole has to be made by the central agency.

(4) The nuisance of fly breeding and offensive smell are naturally objected to.

(5) Even though the amount required for the installation and maintenance of the latrine is not large, it is by no means inconsiderable in relation to what remains, (if indeed the family has a credit balance) after paying for the absolute necessities.

(6) From agricultural point of view the bored hole latrines entail loss of valuable organic matter which should be used to enrich the land.

To prevent smell and fly nuisance an innovation has been introduced by Subramanyam* who provides a water-seal as part of the squatting plate on its undersurface. Since reinforcement becomes necessary it means a considerable addition to the cost of the plate (Rs. 7 each), which is a great deal considering the economic position of the rural population. However, the main difficulties are that the amount of water commonly used for ablution purposes does not suffice for flushing out the seal and it causes splashing which is intolerable. So far these plates have not been in demand. More recently a well-latrine has been suggested by him. This consists of a circular squatting plate of cement-concrete, costing about Rs. 8 which is large enough to cover a well, $2\frac{1}{2}$ feet in diameter. Unlike the bored hole, the well need not be dug down to the subsoil water-level. The cost of digging an eight feet deep well is about the same as for a borehole. The advantages claimed for this type over the bored hole latrine are as follows:

(1) No auger is required and the villager himself may dig the hole.

* K. Subramanyam—personal communication.

(2) The larger diameter increases the capacity of the well and the latrine can be used for a number of years by an average family without shifting the position.

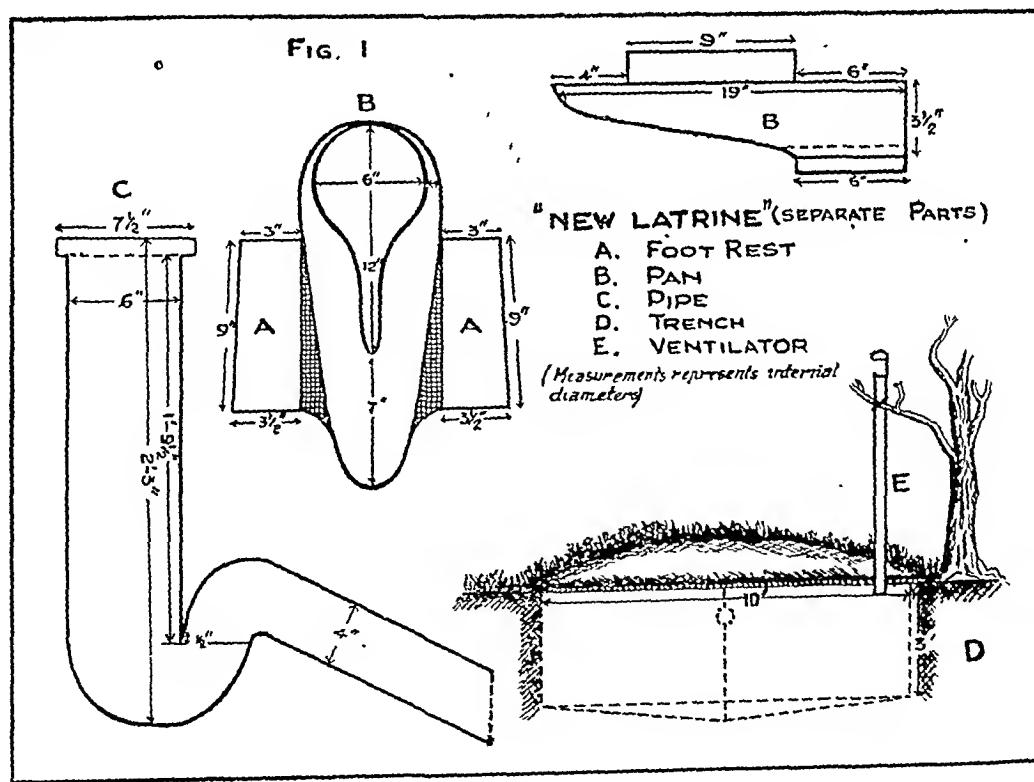
(3) When matured, the manure may be dug out with ordinary farm implements.

An experimental latrine of this type has been constructed.

Since the advantages that might accrue to millions of people over vast regions, from a satisfactory solution of this difficult problem, would be incalculable, in terms of effective suppression of intestinal infections such as cholera, typhoid, dysentery, hookworm and other intestinal worms, increase in wealth (directly and indirectly), improvement of living conditions and general sweetness of rural life, it is most desirable to attempt different methods in the hope that ultimately a completely satisfactory solution will be evolved which, with minor modifications to suit local conditions, might be practicable and effective. The following method is, therefore, suggested :

The new latrine (see figures 1 and 2).—This latrine consists of the following parts: (a) Foot-rests. (b) A pan of the usual water closet, Indian wash down type. (c) A curved pipe. (d) A trench or disposal pit.

first place there is no extra space liable to be soiled which would make it unusable by the next person and in the second place it is cheaper to make. This pan may be made of burnt clay by a local potter, giving a good glaze on the surface or of cement whichever is found cheaper and more suitable for the particular area. In the former case a skilful potter may uniformly turn out the proper shape without unfamiliar apparatus but a really fine pan of the desired thickness and exact shape may be made in a plaster of paris mould by an unskilled worker with a little practice.* All that is necessary is to prepare a slip of the clay of a uniform density and pour it into the mould, adding more slip as required or putting an excess of it in a funnel resting on the hole of the mould. The thickness of the pan is regulated by time. Extra slip is poured out of a hole made for the purpose. Allowing a little time for drying, the mould is opened and the pan is taken out. Glazing material may be applied before or after firing according to the circumstances but in the latter case double firing will be necessary. The glazing material will vary according to the nature of the clay and the temperature attained during firing. The used plaster of paris mould is put away in the sun or in a hot place for drying and when properly dried up it is again avail-



(a) *Foot-rests*.—These may be provided by two burnt bricks which may be partly embedded to fix them in position. Preferably they should be cement plastered, to make them impervious. Alternatively they may be moulded together with the pan.

(b) *The pan*.—This replaces the squatting plate and has two advantages over it. In the

able for use. In the alternative the pan may be made of clay or cement in a wooden mould and the surface may be glazed or smoothened as the case may be. The shape of the pan

*For the suggestion of a plaster of paris mould and for experiments on glazing, the author is indebted to Dr. Atma Ram, Director, Ceramic Institute, Calcutta.

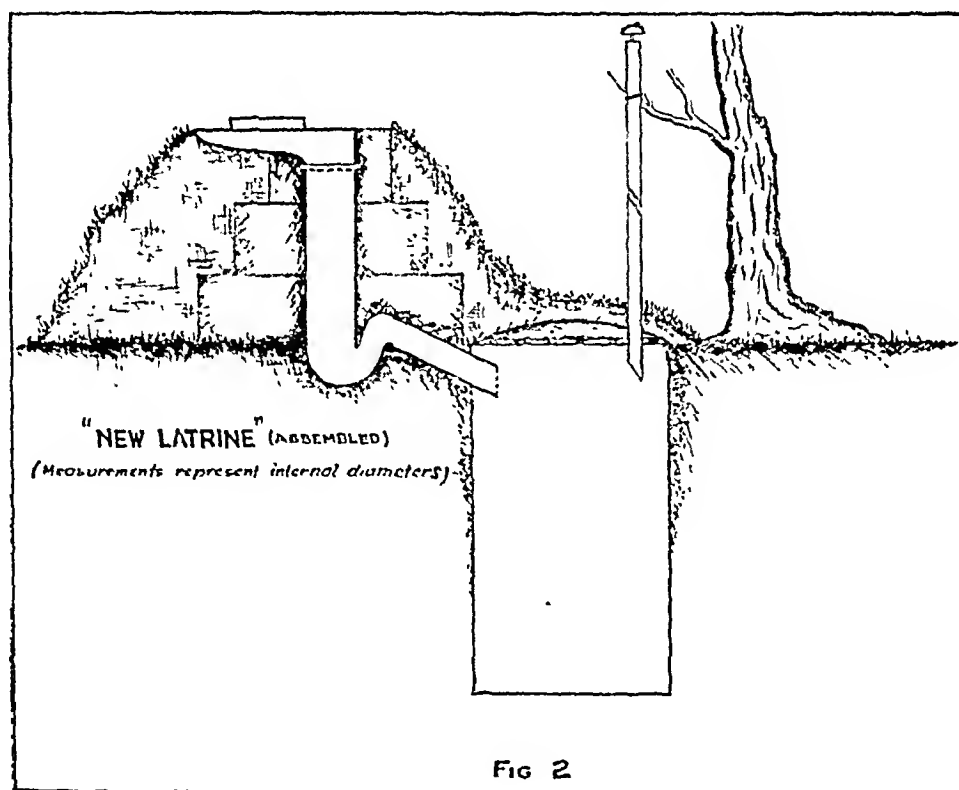


FIG 2

recommended for use in rural areas is shown in figure 1.

There is a circular hole 6 inches in diameter in the pan through which the faeces pass without soiling the walls of the vertical portion of the pipe below. In continuation of this hole there is a long narrow central depression which drains urine, ablution water and other liquid excreta through the hole and also facilitates the passage of faecal matter which might be deposited in the pan through wrong use. The position of the foot-rests is important from this point of view, and it should be carefully adjusted. The most satisfactory results in this respect would be obtained when the foot-rests are moulded along with the pan which could be easily done and when there is a $\frac{1}{2}$ inch rim at the lower end of the hole which fits into the female end of the pipe below.

(c) *The pipe.*—Like the pan, the pipe may be made either out of clay or out of cement as convenient and when required on a large scale, it may be prepared in refractories as glazed stoneware.

Essentially the function of the pipe is to carry the excreta from the pan to the trench 1 foot away but its lateral extension is $1\frac{1}{2}$ feet so that the distal end projects 6 inches beyond the side wall of the trench to prevent erosion. It also provides 2 feet head to ablution or other water used for flushing out the excreta.

The pipe may be made of one of the two shapes described below (figure 3), according to

the quantity of water available for flushing and the price that the user is able to pay.

The two types of pipes are as follows :

1. The simple horn-shaped pipe. The upper or female end receives the bottom rim of the pan and is cemented with it. This is a common feature of both types. Beginning with a diameter of six inches it gradually narrows down to $4\frac{1}{2}$ inches at the distal end and it is curved like a horn as its name indicates. The inner surface (and preferably also the outer surface to increase its life) is well-glazed or smoothed so that the excreta falling on the curvature does not stick and is washed away leaving little or no residual matter on it. In this case, only the small amount of ablution water which the villager normally uses will suffice to keep the pan and the pipe reasonably clean and this action will be further facilitated by the gradually narrowing lumen. The cost of such equipment (including the pan) should be small, possibly not exceeding Rs. 3 if it is made in large quantities. Its simple curvature excludes the possibility of choking through misuse. For these three reasons the simple horn-shaped pipe should find favour with the mass of rural population and should be specially suitable when the latrine is placed in an open place.

2. Water-seal pipe. This will exclude the possibility of trench gases rising towards the seat or pan and therefore there can be no objection to its use in houses provided with internal bath-rooms. About a gallon of water

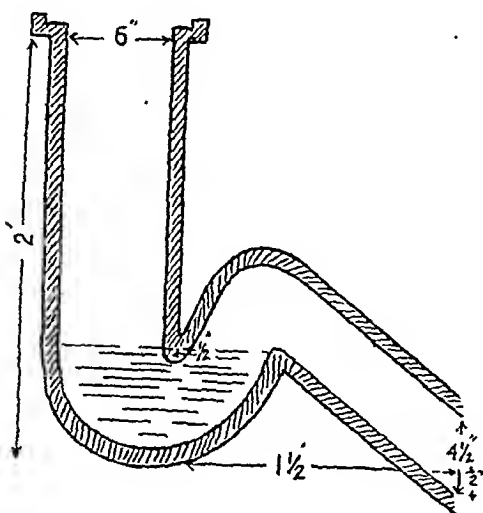
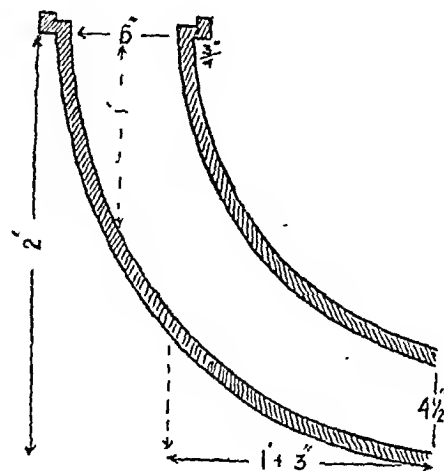
WATER-SEAL
PIPESIMPLE HORN-SHAPED
PIPE

Fig. 3.

will be required to flush out the excreta and this quantity will suffice to induce syphon action and ensure thorough cleaning out. This equipment should not cost more than Rs. 4 when manufactured on a large scale and will be found specially suitable for better trained families who are not likely to choke it up by throwing rags, stones or papers.

(d) *The trench.*—The trench is two feet wide. It is three feet deep at the two ends and $3\frac{1}{2}$ inches deep at the centre where the discharge end of the pipe opens. The length of the trench will depend upon the number of persons using the latrine but, in general, it would be desirable to make it large enough to hold 3 or 4 years' wet sludge. Since the volume of the excreta and the nature of soil and other conditions vary with communities and from place to place no general law can be laid down about the capacity of the trench required. Correct idea can only be gained by actual experience. However, as a rough estimate under Indian rural conditions one might take 9 c.ft. or a little more per adult person as ample provisions. Such a trench will last for 3 to 4 years. To work out the capacity the depth of the trench should be measured up to the opening of the discharge pipe. Roughly a trench 10 feet long will suffice for a family of 6 persons which is the average size for Indian family, for a period of $3\frac{1}{4}$ to 4 years.*

The trench should be carefully covered with seasoned bamboo or strong branches of trees over which palm or other suitable leaves should be spread to hold the earth on the top. The earth should be heaped up and rammed in to form a convex surface over the trench. It may be plastered over with well-puddled clay to prevent soakage and, if necessary, it may be turfed over to prevent damage from rain. The shape of the trench may be rectangular, semi-circular

through percolation and also the fact that the reduction in the volume during the process of digestion is gradual and progressive (having once started the rate of the processes increase rapidly), the volume of indigested stools, together with urine (at the rate of 6 ounces which is passed along with stools) and ablution water would amount to nearly 3 c.ft. at the end of 50 days or 13.1 c.ft. for a family of 6 if $\frac{1}{4}$ of volume is taken to make allowance for smaller amounts contributed by children. For the rest of the year the volume of the sludge for the family would be 10.1 c.ft. In other words, at no time during the year the trench would contain more than 23.2 c.ft. of digested and undigested night-soil including urine and ablution water and therefore a 10 ft. long trench will last for over $3\frac{1}{2}$ years, most likely for 4 years.

In actual fact the trench of this dimension will probably last much longer as indicated from the following calculations. The family in which the 'new latrine' has been constructed consists of at least 10 members, mostly adults. It took 9 months for a borehole latrine of this family to fill up. The capacity of the borehole is estimated at 9.7 c.ft. We are not in a position to say how much difference, if any, would there be in the rates of digestion of night-soil and of percolation of fluid in the two cases, but calculated on the basis of this experience, a 10 feet long trench would take about 7 years to fill up to the level of the discharge pipe, in a family of 6 persons. At any rate, the estimate of 4 years is not likely to be on the high side and experience may show that a smaller trench, perhaps half this size, may suffice for a family of 6 persons. If so, there will be considerable saving in land and in coverings.

* An average Indian adult passes 16 ounces of stools and about 50 ounces of urine. To this volume a quarter of a gallon may be added for ablution water. The process of sludge formation is completed in 25 to 50 days, and the volume is reduced to 0.0021 c.ft. to 0.0073 c.ft. depending upon whether only stools are taken into account or all personal excreta are included. The latter is not likely under rural conditions. However, taking the upper limits and ignoring loss

or of any suitable form according to the availability of land. A ventilating shaft should be provided at a suitable place. This may be made out of a hollow bamboo 8 to 10 feet long which can be tied to a nearby tree to keep it in place. The top of the shaft may be protected from birds by means of half-coconut shell tied to it by means of a stick to serve as a cowl. When the trench has been filled, another may be dug nearby and the seat and the pipe may be turned so that the latter opens into the new trench. In most soils, a period of a year or a little more would be sufficient for complete disintegration of the night-soil and this process may be accelerated by seeding the trench with old night-soil from disused trench or bored hole latrine. When matured, the manure may be dug out from the trench and used in the fields. By alternately using two trenches the process may be carried on indefinitely.

Since the over-ground portion of the pipe is 1½ feet and including the pan it is 2 feet or so, the seat will be in a raised position. Therefore, it should be embedded in well-puddled clay or other suitable supporting material and two steps should be provided to reach the seat from one side. Care should be taken to avoid constructing a platform or any extra space where a person may sit and defecate. If it is desired to place the seat at ground level or any other intermediate lower level, the trench will have to be dug to a corresponding deeper level.

It is important to select the site of the latrine so that there may be no hesitation in using it. In West Bengal, the common sites chosen for defecation are banana plantations, bamboo groves and other waste lands near the house, which are overgrown with vegetation. A bush is often made use of to secure privacy. The new latrine may be put in any of these situations. Privacy may be secured by planting a hedge of a suitable plant, all round the latrine. If necessary or desirable a cover of locally available material may be constructed or other suitable cheap structure may be put up according to the specific requirements of the family.

The cost of the pan, pipe and bamboo to cover the trench is not likely to exceed Rs. 4 for the simple horn-shaped type and Rs. 5 for the other type and Rs. 2 may be added for the cost of digging the trench but in rural communities the users would readily dig it themselves.

The 'new latrine' is primarily intended to serve the rural population in West Bengal. Variations from this standard description may be made to suit local conditions in a given area in respect of the type of pan or seat, the material of which the various parts are made and the type of the disposal pit. For instance, the last may be a circular and deeper hole like the well-latrine but in that case a protective cover will have to be provided. However, the 'new latrine' may be adopted to a great variety of

circumstances. For instance, it could be used for civil and military camping grounds, refugee camps, large or small fairs, pilgrim centres, scattered houses, small towns, wayside railway stations, etc. Better class isolated houses situated in places where public water-carriage system cannot be installed and where some land is available, may also employ the same general plan and, if so desired, use porcelain pans which may be placed in well-constructed bath-rooms inside the houses. In this case the water-seal type is recommended.

The simple horn-shaped pipe is intended for general use in the villages. Using a curved stoneware pipe without a seal a 'new latrine' was installed in a family in a West Bengal village for trial. It has been constantly in use since the 23rd February, 1950. The family members have nothing to complain, in fact, they like it and other families are desirous of installing the same in their homes.

I am grateful to Mr. K. Subramanyam for some useful suggestions, and to Dr. S. C. Seal for assistance in the preparation of this paper.

The Indian Medical Gazette

Fifty Years Ago

MOSQUITOES AND MALARIA IN CALCUTTA

(From the *Indian Medical Gazette*, October
1900, Vol. 35, p. 400)

We have already promised to give some account of Dr. Neild Cook's investigations into the connection between the presence of the anopheles mosquitoes and malaria in the city of Calcutta. The Corporation sanctioned a total expenditure of 'not more than 30 rupees a month', a magnificent sum truly for the Capital of the Indian Empire, for the investigation of a disease which causes more mortality than all other diseases put together. However the sum small as it was, was well spent in the employment of Mahomed Bux and an assistant, the former being somewhat of an expert in the line, having been employed by Major Ross during his special malaria work in Calcutta.

The present report only deals with three months of mosquito hunting, and in that time there have been discovered 89 tanks in Calcutta in which the anopheles larvæ were found in abundance. It is more than possible that many more breeding places will be found during and after the annual rains.

Dr. Cook remarks that the most of the places in which the mosquitoes have been found are tanks, i.e. large collections of water, not merely roadside puddles. The large tanks used for drinking water, or those containing comparatively clean water, were not found infested with the larvæ, but rather those well-known smaller tanks covered with a green scum, only too well known to every resident of Eastern Bengal. Dr. Cook indeed rightly compares them to the dirty duckponds of an English village. Many of these anopheles tanks contained fish and tadpoles, but as a rule where fish were plentiful the anopheles were not so numerous. The anopheles were not found in the very filthy tanks containing practically sewage nor in drains containing sewage, which, however, formed breeding grounds for some varieties of the culex. Anopheles were also found in stagnant ditches, which contained waste water from the overflow of standpipes. Excavations in the ground contained large numbers of larvæ. Towards the east of the Circular Road, which always had the repute of being a most feverish place, a large number of anopheles tanks were found. So far Dr. Cook has not succeeded in finding any anopheles larvæ in any of the numerous paddy fields he has examined, though our readers will remember that Captain S. P. James, I.M.S., of Quilon, has often found them in these situations. Nor has Dr. Cook obtained the anopheles from any wells, though he admits he examined only a few. It is also worth noting that in many places the anopheles larvæ were found with the aid of a tin dipper and a porcelain dish where they were invisible to the naked eye.

Some experiments were made in the extermination of the larvæ with kerosine, but it was found that though the larvæ could be quickly killed by kerosene in pools, unfortunately they reappeared again in about a week. It is also pointed out that it is not an easy matter to cover even the surface of a small tank with kerosene, especially when it contains much vegetation, and the experiments in this direction were by no means a success. Another important point is noted that the mosquitoes do not generally travel far from their breeding place, but 'sit tight under shelter when the wind is strong, so that if they were once exterminated within the town, it is doubtful if they would find their way in again, from the east side of the canal where they are very numerous.'

Dr. Cook concludes as follows: 'All things considered it does not appear probable that any appreciable effect can be made on the prevalence of malarial fevers in Calcutta with an expenditure of 30 rupees a month including pay of establishment, though that has been found sufficient for a preliminary investigation into the prevalence of anopheles'. What we have always advocated is that this experiment be thoroughly tried on a much smaller scale, as in

jails, asylums or similar institutions, and, if successful, attempts on a larger scale might then be made.

Current Topics, Etc.

The Food Habits of *Entamoeba histolytica*

By C. A. HOARE

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 43, July 1949, p. 7)

Most clinicians still regard *Entamoeba histolytica* as an obligatory tissue-parasite, which invades the gut wall, with the production of gross or minute lesions, and feed on erythrocytes and tissue elements. However, there is a steadily increasing number of workers who believe that *E. histolytica* can also live as a commensal in the lumen of the gut, without causing damage to its wall and feeding on micro-organisms and other faecal contents. Their views are supported by observations on the behaviour of *E. histolytica* under various conditions of existence. Thus in amœbic dysentery the amœba feeds on erythrocytes while in cases of chronic amœbiasis and in symptomless carriers it ingests various micro-organisms and faecal debris. In experimental infections of rats it shows every gradation from a commensal life, when it subsists on bacteria and cell debris, to true parasitism, when it feeds on red blood corpuscles. In monkeys this amœba usually produces a symptomless infection and feeds on micro-organisms, while in cultures it may ingest starch granules as well. In addition to phagotrophic nutrition *E. histolytica* takes up food saprozoically, by absorption of fluid through the surface of the body.

The host-parasite relationship in human amœbiasis has already been briefly discussed elsewhere to deal with the commensal habits of *E. histolytica* in a separate paper.

Studies on the Effect of the Administration of Pituitary Adrenocorticotrophic Hormone (ACTH) to a Case of Loeffler's Syndrome and a Case of Tropical Eosinophilia

By P. HERBERT *et al.*

(Abstracted from the *Journal of Allergy*, Vol. 21, January 1950, p. 12)

PITUITARY adrenocorticotrophic hormone (ACTH) was administered to a patient with Loeffler's syndrome and a patient with tropical eosinophilia. The ACTH was given intramuscularly in divided doses. A total of 140 mg. and 120 mg. were administered, respectively.

A transient increase in total circulating leucocytes occurred in both subjects. There followed a marked decrease to virtual disappearance of circulating eosinophiles in the patient with Loeffler's syndrome. In the case of tropical eosinophilia, however, although a

decrease in total eosinophiles occurred, the percentage decrease was much less and did not persist.

The relation of these findings to the clinical picture of these two syndromes is discussed.

The blood histamine level was within normal limits even in the presence of high eosinophilia and did not vary with the changes in eosinophile counts.

Relapse in Typhoid Fever after Treatment with Chloramphenicol

By J. N. BRIGGS

(Abstracted from the *Lancet*, i, 21st January, 1950, p. 115)

SINCE there seems to be no definite agreement about the dosage or duration of administration of chloramphenicol ('Chloromycetin'), and in view of the few cases so far treated with it, the following case is reported:

A case of typhoid fever treated with 16.5 g. of chloramphenicol in five days relapsed eight days after the end of the course, but a second course of 19.5 g. in six and a half days led to complete recovery. The patient developed a low temperature and a coarse tremor during the first course; these may have been toxic effects of the drug but they did not recur in the second course.

The Effect of Rigid Sodium Restriction in Patients with Cirrhosis of the Liver and Ascites

By W. J. EISENMENGER *et al.*

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. 34, August 1949, p. 1029)

THE results of rigid NaCl limitation in the diet of thirteen patients with cirrhosis of the liver and long-standing ascites are presented.

Ascites formation ceased for three months in twelve of the thirteen patients. Urine output increased in each case commensurate with decreased fluid retention.

Four patients did not reform ascites when a normal NaCl intake was tried after three months; eight patients did reform ascites.

Serum protein levels showed a rise following therapy. This is explained primarily on the basis of retention in the serum of protein which previously had been lost in the ascitic fluid.

A high protein and high calorie diet could be maintained despite rigid salt limitation.

A New Method of Diagnosis of Kala-azar

By N. G. S. RAGHAVAN

(Abstracted from the *Indian Journal of Malaria*, Vol. 3, June/September 1949, p. 199)

1. A FINGER PRICK capillary blood test method for the diagnosis of kala-azar by applying Napier and Chopra tests is described.

2. The advantages of above are :—

(a) Vein puncture is avoided.

(b) Quantity of blood to be tested is small.

(c) The method is simple requiring little equipment and is easy to carry out in rapid surveys.

3. Modification of Napier and Chopra tests by addition of eosin brings out the reactions more perceptible and differences between positives and negatives are easily distinguishable.

4. The failure of eosin to diffuse through a column of 'flocules' formed in a positive 1 in 10 saline diluted kala-azar serum and 4 per cent urea stibamine might be taken as ancillary in correlating Chopra tests

5. The results set out here are perforce of a preliminary nature on account of limited facilities available, especially in the matter of intermediate grade enses of kala-azar being not available.

A Case of Cutaneous Amœbiasis

By W. ARMSTRONG

(From the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 43, July 1949, p. 79)

IN the course of some years' medical practice in the New Hebrides I have seen two patients suffering from cutaneous lesions which appeared to be due to amœbiasis (*Entamoeba histolytica*, presumably).

This patient came into hospital in April 1947, with a fungating mass over his sacrum. The first impression was of a fungating sarcoma. The growth was coarsely papillomatous with copious offensive discharge filling the interstices of the growth. The history given was that it started nearer the anus about 3 years before when he was working on another island as part of a labour force recruited by the American military forces. He had received no treatment (probably had not reported sick). At the time I first saw him the area between the lesion and the anus was clear of papillomata but showed evidence of scarring. The discharge was rich in amœbæ.

The patient was immediately put on a course of emetine grain 1 per diem and the local lesion dressed with a 1 per cent solution of carbarsone. Discharge ceased within 3 or 4 days and the carbarsone dressings were replaced by a paint of salicylic acid in tinet. benz. eo. Emetine was continued for 10 days. During the rest of his stay in hospital the area remained dry but the salicylic acid paint was very slowly, if at all, effective in reducing the area of the warty mass. Recourse was then had to glacial acetic acid, which rapidly cleared the area.

Latest information, in May 1948, is that there has been no recurrence.

Kala-azar : Relapse following Splenectomy

By T. C. MORTON

(From the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 43, July 1949, p. 8)

THIS patient contracted kala-azar in Calcutta in December 1945. He received numerous courses of urea stibamine, pentostam, pentamidine, neostibosan and carbostibamide but in spite of extensive treatment his condition gradually deteriorated. A sternal marrow smear in August 1947 was negative but a splenic puncture 3 days later was full of *Leishmania*. It was

considered that the spleen was the main reservoir of infection and it was decided to begin a course of carbostibamide and in middle of the course to remove his spleen, continuing with the course as soon as his condition permitted. This was carried out in August 1947, and after the splenectomy the course of carbostibamide was completed and a fortnight later a further course of pentamidine given. The patient became completely apyrexial a fortnight after his operation and a sternal marrow smear and culture were negative 3 months later. He returned to work but reported monthly for a clinical examination and blood count which remained satisfactory for 16 months. His total red cell count was over 5,000,000 with an average total white cell count of 10,000. A lymphocytosis of from 55 to 65 per cent was, however, present and as this had been reported as a sequel to splenectomy it was not considered significant. He remained completely apyrexial and played football regularly. In January 1949, his total red cell count was found to have dropped to 4,300,000 and in spite of his protests he was admitted to hospital for investigation. A sternal marrow smear showed numerous *Leishmania* and although no lymphadenopathy was present an inguinal lymph gland biopsy was carried out. Sections from this lymph gland were exhibited showing innumerable *Leishmania* present in the reticulum cells. The astonishing feature in this case is the remarkable latency of the disease and the absence of pyrexia together with the excellent physical condition of this patient

The Treatment of Falciparum Malaria with Intramuscular Chloroquine

By C. G. SPICKNALL *et al.*

(From the *American Journal of Medical Sciences*, Vol. 218, October 1949, p. 374, as abstracted in the *International Medical Digest*, Vol. 56, January 1950, p. 7)

THE writers have treated 8 patients with falciparum malaria with chloroquine intramuscularly. All of these patients acquired their infection in Africa and 6 had received suppressive therapeutic quinacrine or quinine prior to admission to the hospital. The longest period that elapsed between the last administration of antimalarial drugs and treatment with parenteral chloroquine was 42 days; the shortest was 12 days. After the diagnosis was confirmed by blood smear each patient was given an intramuscular injection of 0.2 gm. of chloroquine base in 5 cc. of sterile unbuffered aqueous solution according to the method of Culwell *et al.* One patient received an additional dose of 0.2 gm. intramuscularly three days after initial administration of the drug. Daily parasite counts were done on each patient and two to five days later each patient was given a routine course of oral chloroquine.

No adverse local or systemic effects from the intramuscular chloroquine were observed in any of these patients; toxic effects following the parenteral administration of quinine or quinacrine are not infrequent. Rapid clearing of the parasites from the peripheral blood occurred although none of the patients had very high initial parasite densities. The most striking feature of treatment with parenteral chloroquine in this series was that in 6 of the 8 patients no asexual falciparum parasites were found in the blood after administration of the initial dose. The remaining 2 patients showed only some ring forms on the morning of the day further therapy was given. It is likely that the blood of these patients would likewise have cleared completely if further therapy had been delayed. Four of the eight patients showed gametocytes

in their smears after their blood was free of asexual parasites. Neither the intramuscular nor oral chloroquine had any apparent effect on the sexual forms.

The clinical response of these patients to intramuscular chloroquine was likewise very striking. All of them became completely afebrile in one to two days and were markedly improved subjectively. Nausea and vomiting which had occurred in 3 patients subsided promptly following the initial therapy.

The effect of previous antimalarial medication in these patients cannot be definitely determined. It is not likely, however, that this medication had any effect on their response to intramuscular chloroquine since there was a period of from 12 to 42 days from the time the patients last took quinine or quinacrine until chloroquine was given.

It has been recommended that malaria with persistent vomiting, coma, impending coma or a high density of falciparum parasites in the blood smears (5 per cent or more of red cells infected) be treated with parenteral antimalarial drugs. Although none of the patients in this series showed a high parasite density, 3 of them had nausea and vomiting severe enough to prevent administration of oral medication. None of the patients had symptoms of cerebral malaria nor were any in coma. Since none of the writers' patients were critically ill, no definite conclusions can be reached as to the route of administration of the drug in this type of patient. One writer suggested that chloroquine could be given in a saline infusion intravenously over the course of three to four hours for the treatment of patients critically ill with falciparum malaria as carried out by Machella *et al.* with quinacrine and SN 6911. The parenteral administration of chloroquine is not recommended for patients who can take the drug by mouth except for those who show very high parasite densities, as the absorption of chloroquine from the alimentary tract is usually very rapid.

Aureomycin in the Treatment of Infectious Diseases

By H. M. ROSE AND OTHER

(From the *American Journal of Medicine*, Vol. 7, October 1949, p. 532, as abstracted in the *International Medical Digest*, Vol. 56, January 1950, p. 8)

THE writers discuss the use of aureomycin in the treatment of infectious diseases.

Protozoal diseases.—Rapid cures have been reported in 14 cases of amebic colitis with aureomycin by mouth. Symptoms rapidly subsided and the stools became negative in a few days. Strains of amebas isolated from three of these were exposed to the drug *in vitro* and it was shown to have an amebicidal effect.

Diseases due to spirochaetes.—Two cases have been reported of acute syphilis in which the patients were treated orally with aureomycin. Results generally comparable to what would be expected with penicillin were obtained.

Bacterial diseases.—Coccal infections: Some workers treated 4 patients with pneumococcal pneumonia with aureomycin and reported results entirely similar to those obtained with penicillin. The present writers have had the same experience. Excellent results have been described in 1 case of meningococemia. In regard to 60 cases of gonococcal urethritis, however, findings were different, and although the drug was effective it was distinctly inferior to penicillin. It may be remarked, however, that small doses were administered in many of these cases.

Some workers have reported the successful use of aureomycin in localized staphylococcal infections including 2 cases with positive blood cultures.

'Bacillary infections.'—Among the most brilliant effects of aureomycin are those recorded in the treatment of brucellosis.

'Tularemia also responds very favourably to treatment with aureomycin.'

'In view of its antibacterial powers *in vitro* it is not surprising that aureomycin has been tried in a number of infections due to members of the colon typhoid group.' The writers have been unimpressed by the action of aureomycin in severe infections outside the urinary tract due to *Ps. aeruginosa* and Friedländer's bacillus in particular.

Disappointing experiences with typhoid fever and Salmonella infections have been reported. Some workers concluded that the efficacy of aureomycin in typhoid fever was very much less than that of chloromycetin.

Pulmonary tuberculosis.—Some workers used aureomycin in the treatment of 3 young adult patients with extensive acute pulmonary tuberculosis. 'The drug was administered mostly by mouth in doses of 2.0 gm. to 4.0 gm. daily for periods of from 34 to 91 days. In each case the sputum remained positive for tubercle bacilli and the patient showed no improvement either clinically or by x-ray during the treatment period. All 3 patients had a prompt therapeutic response to streptomycin after aureomycin was discontinued.

'Diseases due to rickettsiae.'—Laboratory studies having indicated a powerful antirickettsial action of aureomycin, it followed that some of the first clinical trials of the agent were in this group of diseases. Since chloromycetin had already been proved to be effective in scrub typhus it was hoped that aureomycin would act similarly. On the whole these expectations have been abundantly justified. Aureomycin has been found to be consistently successful in the treatment of Rocky Mountain spotted fever, in Q fever, in Brill's disease, in typhus, and in rickettsial pox. 'Its action in all these various types of rickettsial infections has been remarkably uniform. Within 24 hours after the first dose there is an obvious change for the better in the patient's clinical condition. He appears brighter, "toxæmia" seems less, the temperature is lower and there is welcome relief of headache. At the end of 48 hours in most instances the temperature has reached normal levels, where it remains, and convalescence proceeds uneventfully. At times this does not take place until the third day but in any case all observers concede that aureomycin interrupts the course of every rickettsial disease thus far studied in dramatic style.'

Diseases due to filterable viruses.—Evidence afforded by laboratory experiments warranted an early trial of aureomycin in lymphogranuloma venereum. The results of treatment in 35 cases have been reported. 'Some of these patients had buboes, some acute proctitis and some rectal strictures. There was a remarkable and surprisingly prompt effect on the buboes. In a very few days they were materially shrunken and follow-up revealed that the remission was sustained. Acute proctitis responded equally well. The proctitis associated with rectal stricture also cleared although the chronic anatomic changes persisted.'

The most unexpected finding in regard to this antibiotic was its curative effect in 'primary atypical' or 'virus' pneumonia. 'Cases conforming to the accepted clinical pattern of atypical pneumonia, many of them with serologic confirmation of the diagnosis and most of them having been demonstrated to be unresponsive to penicillin, have also without exception responded to aureomycin. In general the type of response resembles that seen in rickettsial diseases, particularly Q fever. That is to say, within 18 to 24 hours there

is a definite improvement in the patient's general clinical condition, with lessening of fever, cough, headache and "toxæmia". Ordinarily the temperature reaches normal levels at the end of 48 hours and convalescence proceeds smoothly.' In the writers' experience, if the treatment is stopped at this juncture a relapse will occur but this may again be brought under control by readministration of the drug.

Ocular conditions.—Some workers described the use of aureomycin mainly as a local application in the form of aureomycin borate, 0.5 per cent solution, in a wide variety of ocular infections. 'Excellent results were described in conjunctivitis due to staphylococcus, pneumococcus, *H. influenzae* and Morax-Axenfeld bacillus. Reports of several virus diseases of the conjunctiva and cornea were also included. The drug appeared effective in inclusion conjunctivitis and in 1 case of trachoma. It was also favourably reported in herpetic conjunctivitis. . . . Only 8 of 27 patients with epidemic keratoconjunctivitis appeared to benefit from the treatment but . . . even so, aureomycin was more effective than any other agent thus far studied.'

Miscellaneous conditions.—Seven patients with granuloma inguinale have been treated orally with aureomycin and all of them showed a very satisfactory response.

In the writers' experience as well as in the hands of others aureomycin has had equivocal or negative effects in infective hepatitis and infectious mononucleosis. Although the evidence was not absolutely clearcut they concluded that it was not effective in the common cold. 'It has been tried in a number of conditions of undetermined etiology such as rheumatoid arthritis, Hodgkin's disease, periarteritis nodosa, lupus erythematosus disseminatus, ulcerative colitis and Guillain-Barré syndrome without beneficial results. Its action in herpes zoster appears to be equivocal.' In the writers' experience herpes simplex is unaffected.

A variety of dosage schedules with the oral preparation have been described. The antibiotic is now put up in 250 mg. capsules and it has been the writers' habit to regard 4 gm. per day (1 gm. every six hours) as the 'standard' dose for an acutely ill adult of average size. At times when the condition seemed critical they have increased this to 6 gm. the first day. 'If the result of treatment is favourable this dose is reduced after two or three days to 2 gm. or even lower. If nausea is a prominent feature smaller doses at shorter intervals may be given. The taking of milk, aluminum hydroxide gel, phenobarbital, etc., along with the drug has proved helpful. It is very uncommon to be compelled to discontinue treatment altogether on account of nausea.

'For intramuscular injection 30 to 50 mg. of the drug in 3 to 5 ml. of fluid together with procaine may be given at six hourly intervals. . . . This is a painful proceeding and if buffers are employed to diminish the acidity it must be remembered that the antibiotic rapidly loses its potency in solution at a neutral or alkaline reaction. A new vehicle for its intravenous administration, L (—) leucine, has recently been introduced. . . . In 5 ml. of this diluent (containing 131 mg. of leucine) 100 mg. of aureomycin hydrochloride may be dissolved. This can be injected directly at a very slow rate or added to an infusion of isotonic dextrose or saline. As much as 400 or 500 mg. every 12 hours may be given to very seriously ill patients. On the whole, oral administration has obvious advantages.'

'Oral administration of aureomycin is frequently accompanied by nausea and occasionally by vomiting and a metallic taste in the mouth. Females appear more susceptible than males; more than half of the women patients may be quite distressed by these manifestations although their intensity usually diminishes if treatment is continued. The drug also has a slightly laxative action and the passage of an increased number of soft, bulky stools is frequently observed. True diarrhoea is extremely rare.' The

writers have observed 3 instances of transitory vaginitis and a small number of cases of glossitis.

In the writers' clinic 1 case of complete neutropenia occurred in a dermatologic patient after prolonged administration of aureomycin.

Continuous Antibiotic Therapy : A New Method for Home and Office

By N. STEINBERG

(Abstracted from the *Journal of the American Medical Association*, Vol. 142, 21st January, 1950, p. 173)

ONE of the problems of the practitioner is how best to maintain effective blood levels of penicillin or streptomycin when treating the more resistant infection in the home and office. Although the majority of infectious disorders respond to repository penicillin preparations administered once daily, Tompsett and co-workers suggest that suppurative complications in pneumonia are less likely to occur when penicillin is administered at frequent intervals. Waldbott, reporting on the control of infections in asthma, states that he prefers the frequent administration of crystalline penicillin to the use of aerosol or injections of procaine penicillin. Herrel warns against treating severe infections such as bacteremia with injections of penicillin either once or twice daily.

However, in order to obtain the nursing care necessary for the administration of penicillin or streptomycin at frequent intervals, hospitalization is usually mandatory. If for any reason this is not possible, a new method of antibiotic therapy is offered, which, after having been given a thorough trial during the past three years, has proved to be advantageous in the treatment of infectious disorders, as encountered in home and office practice.

DESCRIPTION OF INSTRUMENT

In order to overcome the obvious difficulties in the application of continuous antibiotic therapy in the home and office, an instrument was devised which, fitting about a conventional 5 cc. syringe, automatically limits the travel of the plunger. It is composed of three separable parts: a syringe holder, a sandwich clasp and a wire rack. When these are placed on a 5 cc. syringe (preferably graduated to 6 cc.), they complete the instrument known as a multidose injector. This device is constructed to deliver twelve individual 0.5 cc. doses. Around the instrument is placed a plastic (lucite) guard to prevent breakage and possible injury. For additional protection only, the security bead needle, 7/8 inch (2.23 cm.) in length and 21 or 20 gauge, is used. It is bent and covered with a piece of white rubber tubing to limit depth of penetration beneath the skin (diagram in the original).

METHOD OF USE

The syringe is filled with solution of penicillin or streptomycin or both combined. The area of needle insertion, along the midline of the anterior surface of the thigh or within 2 inches (5.08 cm.) of the median line and approximately 5 inches (12.70 cm.) above the knee, is prepared with aseptic technique. With the syringe held firmly, the skin is punctured with the needle to a depth of $\frac{1}{4}$ inch (0.64 cm.), and an alcohol sponge is placed about the site of entrance. Six strips of adhesive tape (preferably hypo-allergic) 1 inch (2.54 cm.) wide and 9 inches (22.86 cm.) long are then used to fasten the instrument to the thigh. A strip which encircles the back of the thigh is used during the summer months. Three lengths of adhesive are placed in position. The fourth length of adhesive has

a V-shaped piece cut from its centre and is tucked beneath finger grasps. The plastic guard is then placed over the apparatus, which is fastened in position by an elastic belting that encircles the thigh. As a final step two additional adhesive lengths are placed in position.

To administer the medicament, the patient is advised to trip the uplifted end of the lever and press down hard on the plunger. This is repeated at regular intervals, usually every two hours. Unless seriously ill, the patient or a member of the family is told to inject a double dose at midnight and at 4 a.m., omitting the 2 a.m. and 6 a.m. doses. Doses of 500,000 to 2,000,000 units of crystalline penicillin and 0.5 to 1 gm. of streptomycin, singly or combined, dissolved in 6 cc. of distilled water, may be thus administered in fractional amounts during twenty-four hours.

This method was readily accepted by the majority of patients with few reservations. Wagner and Pearce, using this apparatus, have shown that blood levels obtained with penicillin and streptomycin are similar to those obtained through separate intramuscular injections. Furthermore, studies conducted with the more thermolabile antibiotic drug, penicillin, revealed no measurable destruction of this drug in aqueous solution when retained in a syringe lying on the thigh for twenty-four hours.

Clinical and Biochemical Studies in Cholera and the Rationale of Treatment

By M. H. GHANEM AND OTHER

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. 43, July 1949, p. 81)

I. DEHYDRATION is the main process governing the degree of clinical severity of cholera cases. The grading of dehydration, as measured by the clinical criteria mentioned, is as efficient in this respect as delicate laboratory procedure demonstrating blood concentration, the best of these is the specific gravity of plasma.

II. Although the degree of dehydration depends mainly on the number of bowel evacuations rather than their duration, yet it appears that some patients are more easily dehydrated than others. This gives the clinical measure of dehydration, as outlined here, more significant in calculating the amount of fluid needed for its correction. Clinical dehydration is the result of both blood concentration and tissue dehydration.

III. The clinical results of dehydration are due to loss of both water and salts; the former is more important in this respect as no special clinical manifestations could be ascribed to salt depletion alone. This statement indicates the use of isotonic saline with or without glucose in the treatment of these cases and gives no support to the use of hypertonic saline.

IV. Toxins seem to take part in the clinical manifestations of this disease mostly in relation to circulatory failure and anuria. In addition, as a result of this work, toxemia has also to be blamed as partly responsible for some of the biochemical changes found, e.g. azotemia.

V. The following physico-chemical changes were found in the cases of cholera studied and their mechanisms discussed:—

1. *Specific gravity of blood*.—Most of the cases with moderate or marked dehydration showed definite rise in the specific gravity of blood (13 out of 23). Because the figures on admission were higher than

normal in only six of these cases due to associated anemia, a single determination before treatment is considered unreliable as a sign or measure of the degree of blood concentration.

2. *Hematocrit value.*—The same fallacy applies here. Only three showed higher figures than normal on admission owing to variability of the red cell volume and the frequent occurrence of some degree of anemia in this undernourished class of patients.

3. *Specific gravity of plasma.*—All the cases with clinical dehydration showed higher specific gravity of plasma on admission than normal (15 out of 23); only six of these showed high specific gravity of the blood. This illustrates the value of this determination as an index and measure of the degree of blood concentration.

4. *Plasma proteins.*—Hyperproteinemia is evident in two-thirds of cases, obviously the result of hemoconcentration. In the remaining one-third, hypoproteinemia, probably the result of protein loss, was demonstrated. Plasma protein determination is of value for indicating plasma transfusion; the parallelism of the plasma specific gravity with the amount of plasma proteins shows that the former is of value, being simpler, for this determination.

5. *Blood urea.*—Azotemia was demonstrated in two-thirds of the cases studied; it has no relation to the clinical severity, it disappeared in all but three cases under treatment. Although it is mainly related to dehydration and circulatory failure, it has no relation to the degree of blood concentration, or hypochloremia. A renal factor of toxic nature in the production of azotemia is suggested by the present work.

6. *Blood sugar.*—Hyperglycemia was evident in more than two-thirds of the cases, its degree corresponds with the degree of blood concentration which is the main factor in its production. Hypoglycemia was present in only two cases.

7. *Blood potassium.*—Contrary to previous statements diminution of blood potassium was demonstrated in the majority of cases (18 out of 22). It bears no relation to the clinical severity, and it was not responsible for any special clinical manifestation, no hypotonic phenomenon was found. It is probably due to excessive potassium loss in the absence of intake. The saline-glucose treatment was not sufficient to raise the blood potassium in these cases to normal.

8. *Blood and urine chlorides.*—The blood chlorides were markedly increased on admission in all cases examined (16 cases). The higher the figures of blood chlorides the more the degree of dehydration. This hyperchloremia occurred in spite of salt depletion and thus is unreliable as an evidence of chloride disturbance. Contrary to previous statements no hyperchloremia was found. On the other hand, the urine chloride estimations show their value as a definite indicator of the presence and degree of tissue salt depletion so long as the kidney function is not appreciably impaired. The urine chlorides were markedly diminished in all cases examined, taking into consideration the amount of urine passed; it was 3.5 grammes per litre or less in the majority of cases. We feel that urine chloride estimation is not only of value as a measure of the amount and urgency of saline infusions but also guides the progress of saline treatment.

PROGNOSIS IN CHOLERA

(1) The degree of dehydration and its duration, and the availability of proper energetic treatment. If severe and prolonged, dehydration may lead to irreversible cellular damage in addition to the effects of toxemia and anoxemia.

(2) Anuria is a bad prognostic sign needing energetic treatment, even then six out of nine cases of anuria did not respond to the above treatment and died.

(3) The degree of disturbed circulatory dynamics as measured particularly by the venous pressure; patients with very low or unmeasurable venous pressure are bad risks.

TREATMENT RECOMMENDED

Treatment should start immediately the patient is seen even at home.

1. Avoid any effort during the transfer of the patient; immobility in bed should be insisted upon, even during defecation and vomiting.

2. Warm the patient with blankets or hot water bottles for a short time. Energetic heating by electric baths, etc., is condemned.

3. Bandage the limbs as a first-aid measure.

4. Nothing by mouth until the gastro-intestinal irritation is alleviated.

5. *Stimulants.*—Coramine is given as soon as the patient is seen. The use of the other stimulants is left until the clinical examination decides their indications.

6. Careful nursing is of paramount importance; continuous and thorough observation of the patient's condition is essential.

7. *Fluid therapy.*—This should be started immediately the patient is seen together with the preliminary supporting treatments. Fluid administration if guided precisely (in quantity and quality), in the light of combined sound clinical judgment and adequate repeated laboratory data, gives marvellous results, while insufficient or improper use of fluids leads to grave consequences. The guides to proper fluid administration as regards quantity and quality are:—

(a) The degree of dehydration and clinical grading mentioned in this work is sufficiently accurate.

(b) Blood pressure estimation gives us a preliminary idea of the degree of disturbances in the circulatory dynamics, and whether compensatory vasoconstriction is present or not. But as shown in another paper estimation of the venous pressure is the most accurate criterion of the affection of the circulatory system and thus the lower the venous pressure the more energetic the treatment should be.

(c) The degree of blood concentration, estimation of the specific gravity of plasma is the most accurate, simple and rapid method for this purpose. The more the blood concentration the more rapid infusion is indicated to correct blood volume; also the specific gravity of plasma indicates whether plasma is specifically needed or not; if low or normal, plasma transfusions are indicated.

(d) The amount, reaction and chloride content of the urine collected 8-hourly. This procedure gives information on the degree of dehydration, the presence or absence of acidosis, and the degree of salt depletion; acidosis indicates alkali administration, while the amount of chlorides in repeated samples governs the nature (isotonic or hypotonic) and the amount of saline solution to be continued.

Blood urea estimation.—Azotemia indicates restriction of proteins and energetic correction of the blood volume and the disturbed circulatory dynamics; repeated estimations are needed to guide the continuation of these measures.

The amount of fluid needed.—This depends mainly on the degree of dehydration as measured clinically and by the specific gravity of plasma denoting the degree of blood concentration; these usually go hand in hand. Maddock and Coller believe that the presence of clinical signs of dehydration indicates a loss of 6 per cent of body weight; thus a man weighing 70 kg. may be assumed to have a negative balance of 60 cc. per kg. body weight, or a total of about 4,200 cc.; thus 60 cc. of fluid are to be given per kg. body weight per day to this patient. In the cases studied in this work we found the amount of fluid

standard of school hygiene and procedure for guarding educational establishments from the outbreak and spread of preventable infectious diseases. In this the eleventh edition the code is issued in the form of a handbook. The first few sections of the book deal with medical administration, basic principles of health, disinfection and notification of diseases. Then comes the section on communicable diseases, arranged alphabetically, each being treated with reference to its recognition, ætiological agents, source of infection, mode of transmission, incubation period, period of communicability, susceptibility and immunity, prevalence, methods of control and return to school. The book is handy for quick reference and should be useful to school-doctors and teachers.

R. N. C.

A TEXTBOOK OF BACTERIOLOGY.—By N. G. Pandarai, M.D., D.T.M., F.R.C.P. (Edn.). 1948. The Bangalore Printing and Publishing Company, Limited, Mysore Road, Bangalore City. Pp. 748. Price, 18s.

THERE has been no recent publication of any textbook on Bacteriology by an Indian author. De and Chatterjee's book was very popular but, unfortunately, is now out of print. This new book is, therefore, very welcome. It has been written particularly for the undergraduate students. The subject-matters have been presented in a systematic manner, concisely, with up-to-date information. Special attention has also been given to the application of Bacteriology to the clinical and preventive aspects of Medicine. As pointed out by the author, the book suffers from inadequate illustrations with pictures, but this was unavoidable under the conditions in which the book was published. The reviewer is in general agreement with the views expressed by the author in the book with a few exceptions. For example, the non-lactose fermenting intestinal organisms are included under genus *Bacterium* but in recent years they are usually included under *salmonella* and *shigella*. The book can be strongly recommended to the undergraduate students as well as to those going for D.T.M. or D.P.H. course.

S. C. G.

DISORDERS OF SEX AND REPRODUCTION: ÆTIOLOGY, DIAGNOSIS AND TREATMENT.—By A. P. Pillay, O.B.E., M.B., B.S. 1948. H. K. Lewis and Company, Ltd., London. Pp. xiv plus 299. Illustrated with 5 photographs on 2 plates and two graphs. Price, 18s.

THIS book gives most of what is left unsaid, on matters of sex, in medical education.

The items discussed include Anatomy and Physiology of Sex, Problems of Sex, Classification of Sex Disorders, Role of Endocrines in Sex Disorders, Hyperæsthetic Disorders, Anæsthetic Disorders, Sexual Neurasthenia, Sterility and Artificial Insemination.

The treatment includes all details. One may not agree with all recommendations, e.g. cunnilingus for frigid women. Such women should be discarded in the interest of eugenics: They show atavism and are more animal than human.

The real value of the book lies in 69 cases given in appropriate places within the bounds of the book. They reveal many mysteries including the satisfaction derived by pathics.

The paper, printing and binding are good. No printer's errors attract attention. The price is reasonable.

A useful publication.

S. D. S. G.

BOOKS RECEIVED

1. Rural Medicine Practitioner. Vol. 1. No. 1. September 1950. Editor: Dr. R. L. Soni. Printed and published by Dr. Rattan Lal Soni, at Co-operative Press, Railway Road, Ambala City, from the office of Rural Medical Practitioner, Khattarwara, Ambala City.

2. Bulletin of the School of Medicine. University of Maryland. Vol. 35. No. 3. July 1950. Published Quarterly by The Faculty of Medicine, School of Medicine of the University of Maryland. Annual Subscription \$2.00. Medical Alumni Association, University of Maryland, Lombard and Greene Streets, Baltimore 1, Maryland.

Correspondence

PARENTERAL USE OF VITAMINS

SIR,—The parenteral use of vitamins has become widely accepted all over the world, and the number of preparations in general use is growing daily. Doctors and patients have come to regard these preparations as perfectly safe and efficient methods of treatment, and there do not appear to be any contra-indications to their use. This appears to imply in particular to preparations containing the vitamin B-complex. Reports of any untoward results from its use have not been published as far as I am aware. The following occurrence, therefore, seems worth recording.

On 15th September, 1950, a Hindu male, age 40 years, vegetarian, received an intramuscular injection of 1 cc. vitamin B-complex (American manufacture) from a vial from which his wife had already received two or three injections previously. These injections had been tolerated without any by-effect. About five minutes after the injection—the usual care had been taken to make sure that the tip of the needle had not entered a vein—the patient complained of a strong itchy feeling at the site of the injection. Within another minute or so he complained of an itchy feeling within his mouth and soon after also in his face. Very soon a general, intolerable itch was felt over the whole body surface, his face began to swell, his eyes became blood-shot and he became very restless. The patient was given a Trimeton-tablet and 0.3 cc. sol. adrenalin hydr. 1/1,000. As I was at that time still fairly certain that after an injection of this kind no serious reaction could be expected this appeared to be sufficient. However, within another 5 to 7 minutes the general itching became still worse the swelling of the face progressed, and another injection of adrenalin, 0.4 cc, was given. Within the following minutes no improvement was noticeable. The patient who by now had become extremely restless felt the urgent need to go to the bathroom; when he returned he collapsed. His pulse rate was 150 p.m., and the pulse was very feeble. After an injection of coramine intramuscularly this state of collapse abated. There was a profuse outbreak of perspiration. One cc. of adrenalin in oil was given intramuscularly, and 35 to 40 minutes after the offending injection had been given it was evident that the general condition had improved sufficiently to make further active measures unnecessary. Two hours after the injection the face was still swollen and the eyes were still slightly blood-shot, but on the following morning the patient was quite well again, apart from a very mild œdema of the face which disappeared during the day.

It is quite obvious that in this case the injection of vitamin B-complex has acted as a highly potent allergen. Though it is readily admitted that, in spite

of the precautions taken, a small part of the offending agent might have entered a vein, this appears highly improbable for the following reasons: (1) There was definitely no sensation of taste or smell immediately after the injection. (2) The symptoms did not develop suddenly, but slowly after a completely free interval of at least five minutes, and the first symptoms were noticed at the site of the injection.

It is, of course, quite impossible to say what might have happened if energetic counter-measures had not been taken at once. Though it is difficult to believe, from such trivial cause the possibility of a fatal termination cannot be excluded.

The manufacturers state in their directions enclosed with the vial that untoward reactions from the niacinamide of which 10 mg. are present in 1 cc. can be expected, particularly if the solution enters a vein. The reactions following the injection of niacinamide, however, are very different from the sequelae described above and it is improbable that the sequence of events experienced in this case are due to niacinamide alone. The other members of the vitamin B group may as well be responsible for this reaction.

It would be very interesting to hear whether this experience is as singular as one is led to believe from the lack of reports of similar cases in the literature. By a strange coincidence I have been told, after having witnessed such allergic reaction myself, that even more serious reactions have been witnessed of late in Calcutta. If this is correct publication of these reactions would be desirable.

Yours faithfully,

RUDOLF TREU, M.D., L.R.C.P. & S., L.R.F.P.S.

[With regard to the danger of entering a vein unintentionally the reader may go over an article entitled 'The needle in the vein', *I.M.G.*, 75, Feb. 1940, p. 103.—Editor, *I.M.G.*]

CLINICAL HYDROPHOBIA WITHOUT CONTACT WITH RABIES TRANSMITTING ANIMAL

SIR,—The correspondence by Dr. Brooks in your columns of the March issue, referring to my above article (Deshmukh, 1949), which appeared in the *Gazette*, was brought to my notice. Three points mainly emerge from his letter which I will attempt to explain as far as possible.

Firstly, Dr. Brooks appears to disbelieve the fact that I have encountered five cases of clinical hydrophobia where no contact with rabies transmitting animal could be discovered, on the insufficient ground that only few cases are reported so far. To convince disbelievers, I have described in detail two such cases which were admitted to a general hospital and where they were seen and clinically corroborated by a number of doctors besides myself. I have purposely refrained from describing the other three cases which were seen by me alone in private practice and where it was not possible to bring in other doctors to witness. Dr. Brooks seems to agree with us that the reported cases were of clinical hydrophobia, since he has not mentioned his disagreement on the point. Now, from the dates of admission mentioned in the paper, it is clear that they were encountered in a short span of six months. Under these circumstances, I wonder why Dr. Brooks should doubt the occurrence of three other cases during a span of 20 years of my practice, though, I know, that cases need not occur in any definite mathematical order or progression. Even then, the important point at issue is not as to how many cases actually occur without contact with rabies transmitting animals but whether any occur at all and, if so, how? If Dr. Brooks had tried in his letter to enlighten us

on the pathogenesis of such cases, we would have been grateful to him.

It is true that very few such cases are reported in the literature so far, and that was the main reason which prompted me to record these cases, even, as I knew, at the risk of being disbelieved. General practice abounds in numerous surprises and even the present plethora of medical journals would prove inadequate to record all of them. But a large number of these do not reach the medical press because of indifference, shyness, want of time, or fear on the part of the practitioner of being groundlessly discredited or wantonly criticized. This may account for the paucity of the recorded cases.

Secondly, Dr. Brooks contends that my suggestion that 'the virus may remain unattenuated (wrongly quoted by Dr. Brooks as "attenuated") in water and cause infection through abrasions in the mouth' is unacceptable.

In the previous part of his letter he has mentioned a case recorded by Prausnitz where a woman developed hydrophobia as a result of biting off the thread she had used in sewing a garment torn by a rabid dog. Possibility of transmission of hydrophobia by the licking of an abraded surface by a rabid animal has been mentioned by Price (1937) and other authors.

Therefore, I fail to understand why an unattenuated living virus in water cannot be capable of causing infection through abrasions in the mouth as suggested by me.

Thirdly, Dr. Brooks appears to have presumed that I am claiming rats as reservoir host for rabies in India, in my paper. I have not done so, but have only offered for expert consideration a suggestion as to how far would it be feasible to attribute the 'idiopathic hydrophobia' to that susceptible animal which infests almost every house in India. Now that Dr. Brooks has assured us, though without any convincing proof from his own or anybody else's work, of the improbability, the public fears are set at ease. We would have been delighted to thank Dr. Brooks if he had attempted to explain the possible source of infection in the reported cases.

I thank Dr. Brooks for pointing out an inaccuracy of reference in my paper.

P. L. DESHMUKH.

JAYASHREE,
DESHMUKHWADI,
POONA CITY.

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Service Notes

APPOINTMENTS AND TRANSFERS

THE services of Lieutenant-Colonel P. C. Dutta, an officer of the late I.M.S. (Civil), were replaced at the disposal of the Government of the Punjab, with effect from the afternoon of the 18th February, 1950.

Lieutenant-Colonel Jaswant Singh was appointed as Director, Malaria Institute of India, Delhi, in an officiating capacity with effect from the afternoon of the 9th August, 1947, and in a substantive capacity with effect from the 20th October, 1947.

On return from leave, Dr. C. G. Pandit resumed charge of his duties as Secretary, Indian Council of Medical Research, New Delhi, on the 19th July, 1950.

Dr. J. N. Bhattacharji, First Assistant to the Serologist and Chemical Examiner to the Government of India, Calcutta, was appointed to officiate as Serologist and Chemical Examiner to the Government of India, Calcutta, in addition to his own duties for a period of 6 weeks with effect from the 3rd May, 1950 (afternoon), *vice* Dr. Venkataraman granted leave.

Dr. A. L. Bhatia is appointed to officiate in the temporary post of Medical Assistant at the Central Research Institute, Kasauli, with effect from the 5th May, 1950, until further orders.

Dr. C. B. D'Silva is confirmed in the senior scale of the Medical Research Department with effect from the 26th May, 1950.

On return from leave, Dr. K. V. Venkataraman resumed charge of the post of Serologist and Chemical Examiner to the Government of India with effect from the 12th June, 1950. The unexpired portion of his leave is hereby cancelled.

The services of Captain K. A. de'Rozario, Depot Manager, Medical Store Depot, Bombay, were replaced at the disposal of the Ministry of Defence, with effect from the afternoon of the 1st July, 1950.

Shri B. R. Kurl is appointed to the temporary post of Publicity Officer in the Central B. C. G. Organization in the Directorate-General of Health Services, with effect from the 1st August, 1950, until further orders.

LEAVE

Lieutenant-Colonel S. D. S. Greval, lately Serologist and Chemical Examiner to the Government of India, Calcutta, was granted earned leave on average pay for 33 days with effect from the 1st January, 1950.

Lieutenant-Colonel P. A. Dargan, lately Chief Medical Officer, Delhi, was granted earned leave on average pay for 119 days with effect from the 23rd December, 1949. The post of Chief Medical Officer, Delhi, was abolished on the expiry of Lieutenant-Colonel Dargan's leave.

Major N. Jungalwalla, lately Additional Deputy Public Health Commissioner with the Government of India, was granted study leave *ex-India* for a period of 12 months, combined with leave on average pay for a period of 7 months and 23 days, with effect from the 12th May, 1948.

Dr. K. V. Venkataraman, Serologist and Chemical Examiner to the Government of India, Calcutta, was granted leave on average pay for 6 weeks with effect from the afternoon of the 3rd May, 1950.

Dr. C. G. Pandit, an officer of the Medical Research Department on foreign service under the Indian Council of Medical Research, has been granted leave on average pay for 1 month and 8 days with effect from the 10th June, 1950. His services are placed at the disposal of the Director-General of Health Services for the period of the leave.

Dr. C. G. Pandit, an officer of the Medical Research Department on foreign service under the Indian Council of Medical Research, was granted an extension of leave on average pay for 1 day in continuation of the leave sanctioned to him.

Dr. S. N. Chakraverty, a temporary Assistant Depot Manager, Medical Store Depot, Karnal, was granted earned leave for 34 days with effect from the 24th January, 1950, preparatory to the termination of his services.

Shri D. A. Ramawariyar, Factory Manager, Medical Store Depot, Bombay, is granted leave on average pay for 1 month with effect from the 16th June, 1950 to the 15th July, 1950 (both days inclusive), and is allowed to suffix to his leave the 16th July, 1950, being

Sunday and the 17th July, 1950, being a gazetted public holiday on account of Ramzan-Id. It is certified that on return from leave, Shri D. A. Ramawariyar will join the same post at Medical Store Depot, Bombay.

Miss T. K. Adranvala, Chief Nursing Superintendent, in the Directorate-General of Health Services, was granted earned leave for 13 days with effect from the 5th June, 1950, with permission to prefix Sunday, the 4th June, 1950, and to suffix Sunday, the 18th June, 1950, to her leave.

RETIREMENTS

The following officers of the late Indian Medical Service (Civil) have been permitted to retire with effect from the date shown against their names:—

Colonel (Honorary Major-General) Sahib Singh Sokhey. Dated 15th December, 1949.

Lieutenant-Colonel A. S. Garewal. Dated 1st February, 1950.

Lieutenant-Colonel B. N. Hajra. Dated 1st May, 1950.

Colonel S. L. Bhatia. Dated 23rd May, 1950.

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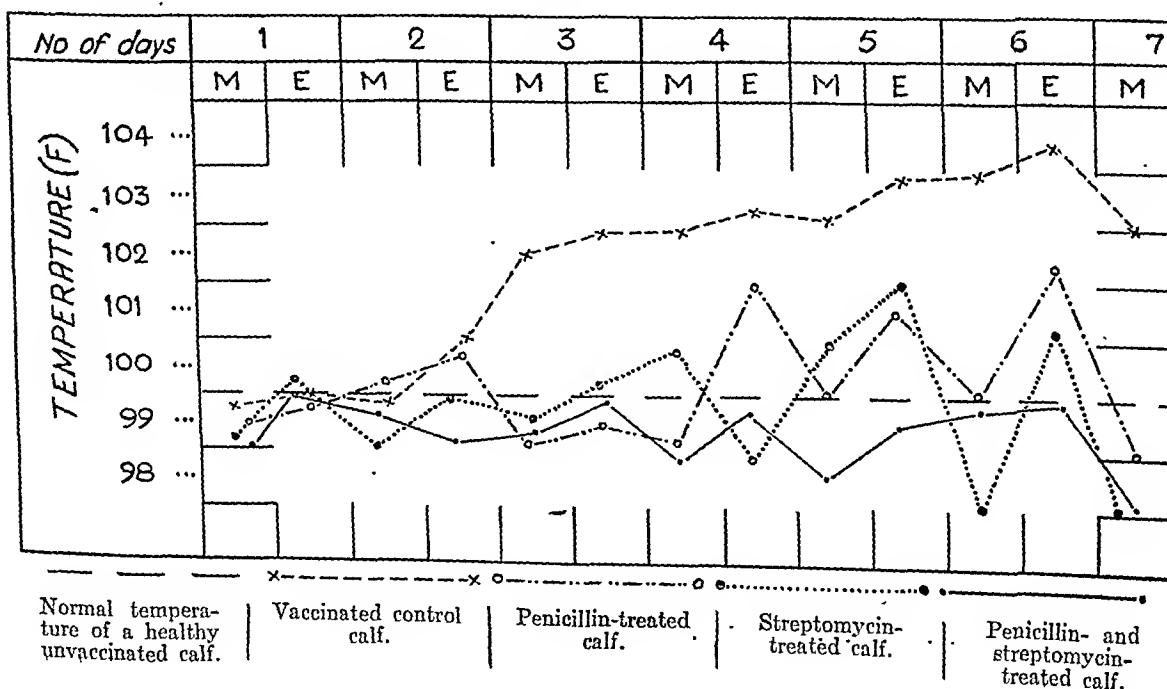
CONTENTS

	Page		Page
ORIGINAL ARTICLES		DRUGS ACT, 1940 511	
Toxic Factor(s) in Vaccinia Virus and its Neutralization by Penicillin. A preliminary communication. By V. N. Krishna Murthy, M.D. 487	487	STUDIES IN ANTIMALARIALS 512	512
Studies of the Urinary Excretion of Nicotinic Acid in Diabetic Patients. By T. H. Rindani and S. N. Narayan Rao 488	488	KOCH AND CHOLERA 512	512
Comparative Value of Sulphadiazine and Sulphaguanidine in the Treatment of Acute Bacillary Dysentery. By Najib Khan, M.D. (Durham), Lieutenant-Colonel 490	490	FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL 512	512
Iliacus Minor. A report. By N. Das and B. Singh 492	492	PUBLIC HEALTH SECTION	
Spontaneous Pneumo-peritoneum. By H. B. Dingley, B.Sc., M.B., B.S., T.D.D. 492	492	Mushroom Poisoning in India. By S. D. S. Greval, Lieutenant-Colonel, I.M.S. (Retd.) 513	513
Barbiturate Poisoning treated with Picrotoxin. By N. R. Konar, M.D. (Cal.), M.R.C.P. (Lond.), and A. K. Das, M.B. (Cal.), D.T.M., M.R.C.P. (Edin.) 494	494	Efficacy of Penicillin in Reducing Bacterial Contamination in Vaccine Lymph. By J. Das Gupta, M.B., D.P.H., D.T.M. 514	514
Argemone and Mustard Seeds. By P. K. Sanyal, Ph.D. (Lond.), B.Sc., Pharm. Chem., Ph.C., F.L.S., F.R.M.S. (Lond.) 498	498	FIFTY YEARS AGO	
Studies on Plasma Protein. III. Malaria. By H. Chakravorti, M.D. (Cal.) 500	500	THE ANNUAL REPORTS OF THE LUNATIC ASYLUMS OF BENGAL, MADRAS AND THE PUNJAB FOR 1899 (<i>Indian Medical Gazette</i> , November 1900, Vol. 35, p. 437) .. 518	
A MIRROR OF HOSPITAL PRACTICE		CURRENT TOPICS, ETC.	
Aureomycin in the Treatment of Pemphigus Foliaceus. A case report. By D. Panja, J. C. Gupta and A. K. Banerji 503	503	RESISTANCE TO PROGUANIL (<i>British Medical Journal</i> , i, 21st January, 1950, p. 171) .. 519	519
EDITORIALS		PARENTERAL NUTRITION IN THE SURGICAL PATIENT AS PROVIDED FROM GLUCOSE, AMINO ACIDS AND ALCOHOL (<i>Surgical Newsletter</i> , No. Wa 277, dated July 1950, prepared by the American Medical Association) 520	520
George Bernard Shaw Passes On 505	505	FOLLOW-UP STUDY OF PATIENTS WITH THROMBO-ANGITIS OBLITERANS (<i>Surgical Newsletter</i> , No. Wa 277, dated July 1950, prepared by the American Medical Association) 520	520
Sulphonamides and Sulphones 506	506	THE NERVE SUPPLY TO THE MAXILLARY INCISORS (<i>Dental Newsletter</i> , No. Wa 283, dated July 1950, prepared by the American Dental Association) 521	521
The Treponematoses 506	506	OBSERVATIONS ON THE PHYSIOLOGIC EFFECTS OF CORTISONE AND ACTH IN MAN (<i>Medical Newsletter</i> , Wa 280, dated July 1950, prepared by the American Medical Association) 522	522
MEDICAL NEWS		RADIOACTIVE PHOSPHORUS IN CHRONIC LYMPHATIC LEUKÆMIA (<i>Medical Newsletter</i> , Wa 280, dated July 1950, prepared by the American Medical Association) .. 522	522
THIRD SESSION OF W.H.O. REGIONAL COMMITTEE FOR SOUTH-EAST ASIA 507	507	PROMACETIN IN TREATMENT OF LEPROSY: PROGRESS REPORT (<i>Medical Newsletter</i> , Wa 280, dated July 1950, prepared by the American Medical Association) .. 522	522
DIRECTORS OF PUBLIC HEALTH MEET IN KANDY 508	508		
WAYS TO RAISE HEALTH STANDARDS 509	509		
W.H.O. NAMES NEW TECHNICAL ADVISER FOR YAWS CAMPAIGN IN INDONESIA 509	509		
CULTIVATING GERMS—TO PRODUCE SULPHUR. By Maurice Goldsmith 510	510		
NEW APPOINTMENT FOR BLIND PHYSICIAN 510	510		
DRUGS RULES, 1945 511	511		

(Continued on page 486)

CONTENTS—(Continued from page 485)

	Page		Page
CLINICAL USE OF THE ANTIBIOTIC CHLORAMPHENICOL (CHLOROMYCETIN [®]) (Medical Newsletter, Wa. 280, dated July 1950, prepared by the American Medical Association)	523	FOLLOW-UP OBSERVATIONS ON THE TREATMENT OF BANCROFTIAN FILARIASIS WITH HETRAZAN IN BRITISH GUIANA. By R. Hewitt et al. (<i>American Journal of Tropical Medicine</i> , Vol. 30, March 1950, p. 217)	528
AUREOMYCIN FOUND TO BE POTENT GROWTH FACTOR AS WELL AS DRUG (17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society)	523		
VAST UNTAPPED FOOD RESERVE FOUND IN CENTRAL AMERICAN PLANTS (17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society)	524	REVIEWS	
EVERY PART OF A CANCER-CAUSING CHEMICAL CAN NOW BE TRACED THROUGH THE BODY (17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society)	525	A TREATISE ON TROPICAL THERAPEUTICS. By Sir R. N. Chopra, B. Mukerji, and I. C. Chopra	528
MODERN AIR POLLUTION CRUMBLING ANCIENT MONUMENTS OF GREECE (17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society)	525	THE RHEUMATIC DISEASES. By G. D. Kersley, M.A., M.D. (Cantab.), F.R.C.P. (Lond.), T.D., with a Foreword by Sir Francis R. Fraser, M.A., M.D. (Ed.), F.R.C.P. (Lond.) Third Edition. 1950	528
DOUBLING HUMAN LIFE-SPAN IN NEXT 10 YEARS POSSIBLE, CHEMIST SAYS (17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society)	525	A SHORT TEXTBOOK OF RADIOTHERAPY FOR TECHNICIANS AND STUDENTS WITH A SUPPLEMENTARY CHAPTER FOR THE DERMATOLOGIST. By J. Walter, M.A., B.M. (Oxford), M.R.C.P. (Lond.), D.M.R.E. (Cantab.), and H. Miller, M.A., Ph.D. (Cantab.), F.Inst.P. Foreword by J. L. A. Grout, M.C., F.R.C.S. (Ed.), F.F.R., D.M.R.E. 1950	529
CHLORGUANIDE HYDROCHLORIDE AND MALARIA (<i>Journal of the American Medical Association</i> , Vol. 142, 11th March, 1950, p. 745)	526	THE EXAMINATION OF WATERS AND WATER SUPPLIES (THRESH, BEAK AND SUCKLING). By Edwin Windle Taylor, M.A., M.D., B.Ch. (Cantab.), M.R.C.S., L.R.C.P., D.P.H. (Lond.) Sixth Edition. 1949	529
CHLORAMPHENICAL IN TYPHOID FEVERS. By M. J. Shah (<i>Indian Journal of Medical Sciences</i> , Vol. 4, June 1950, p. 250)	526	BLOOD TRANSFUSION. By Elmer L. De Gowin, M.D., Robert C. Hardin, M.D., and John B. Alsever, M.D. 1949	529
THORACIC AMOEBIASIS. By A. S. Bookless (<i>Journal of the Royal Army Medical Corps</i> , Vol. 94, February 1950, p. 52)	526	GERIATRIC MEDICINE. THE CARE OF THE AGING AND THE AGED. Edited by E. J. Sticglits, M.S., M.D., F.A.C.P. Second Edition. 1949	530
GANTRISIN IN THE TREATMENT OF URINARY INFECTIONS. By G. Carroll et al. (<i>Journal of the American Medical Association</i> , Vol. 142, 14th January, 1950, p. 85)	526	BOOKS RECEIVED	530
COOLEY'S ANÆMIA. By N. K. Chandra and other (<i>Indian Journal of Pediatrics</i> , Vol. 18, April 1950, p. 89)	527	ABSTRACTS FROM REPORTS	
PAIN IN THE CHEST WALL SIMULATING HEART DISEASE. By D. R. Allison (<i>British Medical Journal</i> , 11th February, 1950, p. 332)	527	THE THIRTY-SECOND ANNUAL REPORT OF KING EDWARD VII MEMORIAL PASTEUR INSTITUTE AND MEDICAL RESEARCH INSTITUTE, SHILLONG, FOR THE YEAR ENDING 31ST DECEMBER, 1948	530
		ANNUAL REPORT OF THE CHEMICAL EXAMINER'S DEPARTMENT, MADRAS, FOR THE YEAR 1949	531
		CORRESPONDENCE	
		TREATMENT OF INFANTILE CIRRHOSIS OF THE LIVER	531
		PALUDRINE POISONING	533
		KALA-AZAR IN INDIA AND THE SANDFLY	534
		SULPHA AND SULPHONE DRUGS	534



influenza virus on the rabbit cornea, Evans and Rickard (1945) have shown that though there is a complete lack of multiplication of influenza virus in the eye of the rabbit yet a severe corneal damage is produced which they attribute to a toxic factor. The rapid death of animals following the injection of either rickettsiae or certain virus preparations leads to the conclusion that the effect is that of toxin and not dependent upon the growth and multiplication of the infecting virus. Henle and Henle (1946) have succeeded in eliciting specific anti-toxins which failed to react with toxins of closely allied viruses. Little work seems to have been done on the toxic factors of vaccinia virus though considerable amount of work has been done on the vaccinia virus particle itself.

This toxic factor of the vaccinia virus, whatever its nature may be, seems to get neutralized by penicillin or a factor associated with penicillin. Penicillin or rather a factor associated with penicillin has been known to neutralize certain endo-toxins of certain gram negative organisms as reported by Hawk *et al.* (1949). This observation is of considerable interest and it is worth while trying a combination of penicillin and streptomycin for smallpox therapy.

Further work regarding the nature of this toxic factor is in progress.

The author is greatly indebted to Dr. T. Chandrasekhariah, Director of Public Health in Mysore, for the necessary facilities for work and permission to send this preliminary report for publication.

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STUDIES OF THE URINARY EXCRETION OF NICOTINIC ACID IN DIABETIC PATIENTS

By T. H. RINDANI
and

S. N. NARAYAN RAO

(From the Department of Physiology, Topiwala National Medical College, Bombay 8)

IN a recent paper, Banerjee, Ghosh and Bhattacharya (1948) have developed a method using Koenig's (1904) basic reaction for the estimation of nicotinic acid in urine in the presence of sugar. It represents a simplification

of the earlier methods of Melnick and Field (1940), Swaminathan (1939), Harris and Raymond (1939) and several others. An interest in the study of urinary excretion of nicotinic acid having been roused by the paper of Neuwahl (1943) in which a marked improvement in glucose tolerance of diabetic patients is reported with the oral administration of nicotinic acid, the present investigation was undertaken to study the extent, if any, of interference in the nutrition of nicotinic acid of diabetic patients with pronounced diminished glucose tolerance.

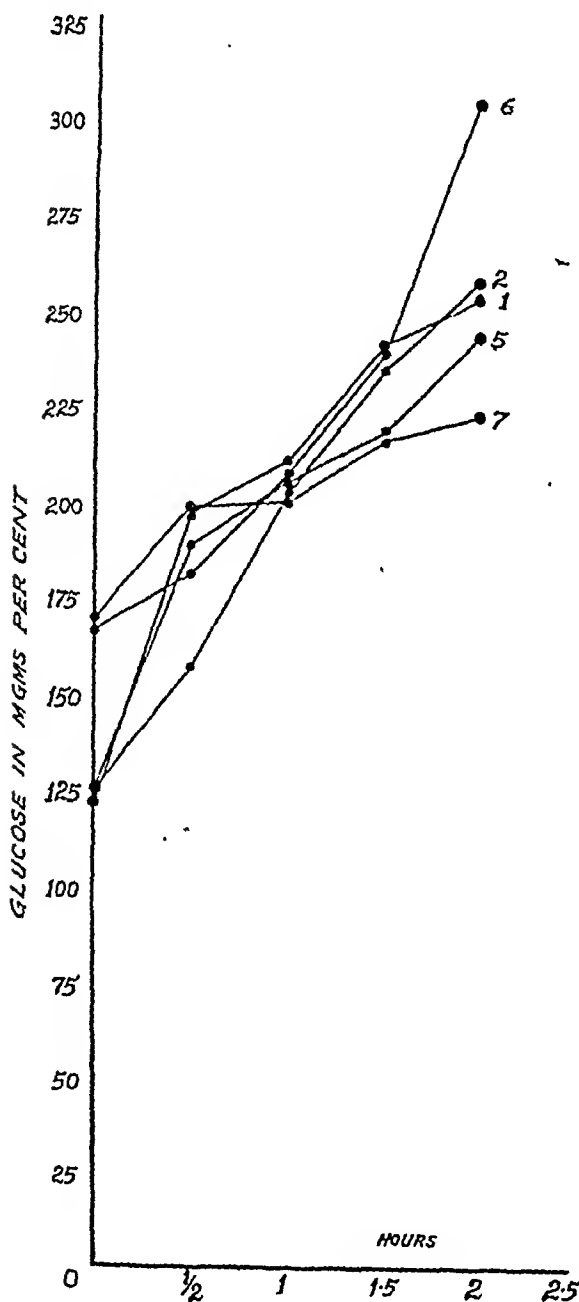
Experimental

Ten subjects with a history of diabetes of two to ten years' duration were chosen for the investigation. All of them were non-smokers, seven were males and the remaining three females, their ages varying from 28 to 63 years except in the case of one subject who was a 14-year-old boy. As regards their diet three were vegetarians and others non-vegetarians.

The urine of each subject voided in a 24-hour period was collected in bottles containing 20 cc. of 50 per cent sulphuric acid. Glucose tolerance tests were also carried out on these subjects, advising them to abstain from food for 12 hours, and orally administering appropriate amounts of glucose and drawing out about 5 cc. of blood at half-hour intervals up to two hours and estimating immediately the sugar percentage by the well-known Folin and Wu (1920) method. Sugar in urine was quantitatively estimated with Benedict's reagent.

The estimation of nicotinic acid was carried out in accordance with the method of Banerjee *et al.* (*loc. cit.*). To 25 cc. of urine in a 250 cc. beaker were added 8 cc. of concentrated hydrochloric acid. The beaker was heated in a water bath and 10 per cent potassium permanganate solution was added till all the sugar was oxidized. In order to remove manganese present in the solution, solid disodium hydrogen phosphate and sodium hydroxide were added. The solution was then digested in a water bath for three-quarters of an hour with 40 per cent sodium hydroxide so that the strength of the alkali was 4 per cent. By making the solution acid with concentrated hydrochloric acid and treating it with potassium permanganate solution, a colourless solution was obtained. The solution was concentrated in order to reduce its volume by heating over the water bath. Afterwards its pH was adjusted to 7 with the use of bromothymolblue as indicator and adding phosphate buffer in the proportion of 6 cc. of buffer to 10 cc. of the solution. The resulting white precipitate was filtered off. In this manner a colourless solution was obtained. 16 cc. of this solution were taken in a 25 cc. stoppered graduated cylinder and in another similar cylinder a dilute solution containing 10 γ nicotinic acid per cc. was taken. 6 cc. of the

Fig. 1.



phosphate buffer (pH 7) were added and the volume made up to 16 cc. To each of the cylinder was added 1 cc. of 4 per cent alcoholic solution of aniline followed by 8 cc. of freshly prepared cyanogen bromide solution. The contents of the cylinders were shaken and allowed to stand for 2 minutes and the yellow colour which developed was compared by means of a colorimeter.

Results and discussion

The results obtained are recorded in tables I and II.

TABLE II

Showing blood sugar amount in half-hourly samples after oral glucose administration

Num-ber	Subject	½ hour, mg. per cent	1 hour, mg. per cent	1½ hours, mg. per cent	2 hours, mg. per cent
1	M. B. M.	192.0	210.0	243.0	251.0
2	M. W.	156.0	203.0	234.0	258.0
3	H. B. A.	197.0	221.0	260.0	290.0
4	N. K. B.	283.0	284.0	303.0	328.0
5	R. K. S.	188.0	204.0	218.0	243.0
6	C. S.	180.0	207.0	243.0	303.0
7	H. S.	192.0	198.0	215.0	220.0
8	M. R. D.	164.0	214.0	244.0	268.0
9	S. K. T.	175.0	219.0	251.0	270.0
10	A. B. R.	140.0	162.0	175.0	190.0

In table II blood sugar percentages obtained show a definite diminished sugar tolerance in each of the subject examined. The sugar tolerance values of two female subjects and three male subjects representing between them subjects habituated to vegetarian and non-vegetarian diets have been graphically shown in figure 1.

The amounts of nicotinic acid excreted per day by the subjects are recorded in the last column of table I. The range is noticed to be between 2.6 mg. and 5.6 mg. These values are very similar to those reported for normal healthy subjects by Ghosh (1941). Thus it

TABLE I

Showing sugar percentage in blood and urine and nicotinic acid excretion in 24 hours

Number	Subject	Sex	Age	Diet	Fasting blood sugar, mg. per cent	URINE		
						Volume, cc.	Sugar, mg.	Nicotinic acid, mg. per day
1	M. B. M.	M.	28	Non-veg.	121.5	2,125	110.0	5.6
2	M. W. . .	F.	45		124.0	1,700	80.0	4.8
3	H. B. A.	M.	63		180.0	1,825	60.0	3.9
4	N. K. B.	M.	14	Veg.	270.0	1,950	130.0	4.1
5	R. K. S.	M.	58		124.0	1,470	52.0	3.5
6	C. S. . .	M.	60		166.0	1,590	110.0	2.8
7	H. S. . .	F.	48	Non-veg.	160.0	2,375	180.0	4.7
8	M. R. D.	M.	32		151.0	1,620	95.0	5.3
9	S. K. T.	F.	56		149.0	1,860	140.0	2.6
10	A. B. R.	M.	41	Non-veg.	162.0	2,100	99.0	4.5

would appear that the nicotinic acid nutrition of diabetic patients is not interfered with. Further studies in nicotinic acid excretion in different conditions such as starvation, diabetic coma, etc., are being pursued.

Summary

By the chemical method outlined by Banerjee *et al.* (*loc. cit.*), the nicotinic acid excreted in 24 hours in urine of ten diabetic patients with a marked diminished glucose tolerance have been studied. The amount excreted per day is found to be between 2.8 and 5.6 mg. as in normal healthy individuals.

We take pleasure in recording our thanks to the Dean, Topiwala National Medical College, for taking keen interest in this investigation.

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COMPARATIVE VALUE OF SULPHADIAZINE AND SULPHAGUANIDINE IN THE TREATMENT OF ACUTE BACILLARY DYSENTERY

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WITH the multiplicity of drugs of the sulpha group, the necessity for a study of comparative value of different members of this group is obvious. The present paper deals with the comparative value of sulphadiazine and sulphaguanidine in the treatment of acute bacillary dysentery. A study was started with the plan to treat alternate cases of bacillary dysentery with sulphadiazine (group 'A') and sulphaguanidine (group 'B'). The total number of patients treated is 191.

Group 'A'—Sulphadiazine .. 82

Group 'B'—Sulphaguanidine .. 109

The difference in the number of the 2 groups is due to the fact that some of the cases

of bacillary dysentery were mixed infection (amebic as well as bacillary) and were, therefore, excluded from this survey.

Diagnosis.—Diagnosis of bacillary dysentery was made on the findings of 'bacillary exudate' in the stool. All stools were cultured: positive stool culture was obtained in 40 per cent of group 'A' cases and 49.5 per cent in group 'B', though the proportions of Flexner, Boyd, Sonne, Smitz and Shiga types were practically same in both the groups.

Clinical facts.—On the average all the patients were ill for approximately one day prior to admission to hospital and they were all diagnosed and treatment commenced on the same day as they were admitted to the hospital. The stool of each patient was examined daily and graphic records kept to record the progress. If pyrexia at the commencement of illness is a criteria of the severity of the infection, 75 per cent in group 'A' were febrile on admission when compared with 50 per cent in group 'B'.

Treatment.—All the patients were kept in bed and given fluid diet. They were all given plentiful drinks of glucose, sodi bicarb, salt and lime juice.

Group 'A' received sulphadiazine 2 gm. to start with and 1 gm. 4-hourly till the total dose of 11 gm. had been given. Group 'B' received sulphaguanidine 6 gm. to start with and 3 gm. also 4-hourly till the total of 60 gm. had been given.

Result.—The result of the treatment was judged by the following criteria:—

- (a) Duration of pyrexia.
- (b) Duration of blood in stools.
- (c) Duration of mucus in stools.
- (d) Duration before stools were 'formed' in consistency.
- (e) Duration before stools became normal.

The duration of stay in the hospital is not taken into consideration as that depended on the availability of beds or otherwise.

Pyrexia persisted for 2.3 days in group 'A' and for 3 days in group 'B' (table I). The stools were on the average free of blood after 1.4 and 1.8 days of commencement of treatment in group 'A' and 'B' respectively. The stools were mucus free 1.8 and 2.5 days, formed 1.5 and 2.3 days, and normal 2.2 and 3.3 days after the commencement of treatment in groups 'A' and 'B' respectively. On the average the patients in group 'A' were placed on the normal diet 4.5 days and in group 'B' 5.1 days after admission to the hospital. The average quantity of sulphadiazine required by group 'A' was 7.25 gm. and sulphaguanidine 33.3 gm. by group 'B'.

It was noted that 8 patients on sulphadiazine had nausea and 3 of them vomited but

TABLE I

						Sulphadiazine group A	Sulphaguanidine group B
Total number treated	82	109
Culture positive	34 (41%)	54 (49.5%)
<i>B. flexner</i>	23	32
<i>B. sonne</i>	4	8
<i>B. boyd</i>	4	7
<i>B. smitz</i>	2	6
<i>B. shiga</i>	1	1
Percentage of patients febrile on admission	70%	50%
Number of days of disease before admission	0.9	0.9
Days febrile after commencement of treatment	2.3	3.0
Days stools free of blood after commencement of treatment	1.4	1.8
Days stools free of mucus after commencement of treatment	1.8	2.5
Days formed stool	1.5	2.3
Days normal stool	2.0	3.3
Days normal diet	4.7	5.1
Quantity of drug required before stools became normal	7.25 gm.	33.3 gm.

in no case was this serious enough to warrant interruption of treatment. No other ill-effects were noticed with the sulphadiazine treatment. With the sulphaguanidine treatment three-fourths of the patients complained of distension

drugs—sulphadiazine as well as sulphaguanidine—as well as the culture positive group. An interesting fact was that the stools were on the average free of blood a little earlier in culture negative than in culture positive series.

TABLE II

		AFTER COMMENCEMENT OF TREATMENT. NUMBER OF DAYS STOOLS									
		Total number of patients treated		Free of blood		Free of mucus		Formed stools		Normal stools	
		A	B	A	B	A	B	A	B	A	B
All patients	..	82	109	1.4	1.8	1.8	2.5	1.5	2.3	2.2	3.3
Culture negative	..	48	55	1.4	1.5	1.9	2.3	1.6	2.4	2.3	3.3
Flexner	..	23	32	1.4	2.3	1.7	2.8	1.6	2.8	2.1	3.5
Sonne	..	4	8	1.0	2.4	1.7	3.1	1.5	2.6	2.25	2.75
Boyd	..	4	7	1.0	1.4	2.0	2.3	2.0	2.1	2.0	2.6
Smitz	..	2	6	2.0	1.25	2.0	2.2	1.1	2.3	2.0	3.2
Shiga	..	1	1	1.0	2.0	1.0	4.0	1.1	3.0	1.0	4.0

Figures in column 'A' for sulphadiazine-treated series and column 'B' for sulphaguanidine-treated series.

and needed some palliative mixture containing tinct. card. co. and tinct. belladonna. The more educated patients usually complained of the large number of pills they had to swallow. In sulphaguanidine series, 3 patients (2.7 per cent) failed to respond to the treatment although to two of them sulphaguanidine 90 gm. was given. All group 'A' cases responded to the usual dose of sulphadiazine. As given in table II, the number of different types of bacillary dysentery cases is too small to allow accurate estimation of comparison of response in each group but the general impression is that Flexner, Sonne and Shiga types responded better to sulphadiazine than to sulphaguanidine. The culture negative group responded to both, the

The economic side of the sulpha drugs when mass treatment of such common diseases like bacillary dysentery is concerned cannot be lost sight of. The comparative cost of 7.25 gm. of sulphadiazine and 33.3 gm. of sulphaguanidine—the average dosages required to cure the dysentery patient—is to be considered. From May & Baker's catalogue, the price of 67 half gramme tabloids of sulphaguanidine in small package is Rs. 5-5-9 and in bulk package Rs. 3-6-3 when compared with the cost of sulphadiazine 15 half gramme tabloids which for the small packing is Re. 1-15-9 and bulk packing Re. 1-10-6. Thus the difference in each case treated with sulphaguanidine and sulphadiazine is Rs. 3-6-0 for individual patients and Re. 1-11-9 for bulk purchasers.

Summary and conclusion.—The study of 191 cases of bacillary dysentery treated alternatively by sulphadiazine and sulphaguanidine is given.

1. Both sulphaguanidine and sulphadiazine are useful in the treatment of bacillary dysentery though 2.7 per cent failed to be cured with sulphaguanidine but responded to sulphadiazine.

2. The speed of recovery is greater with sulphadiazine than with sulphaguanidine.

3. Finding of bacillary exudate in the stools warrants the use of chemotherapy without waiting for the culture report as culture positive as well as culture negative cases respond equally well.

4. On the average 7.25 gm. of sulphadiazine and 33.3 gm. of sulphaguanidine are required for the treatment of acute bacillary dysentery.

5. From the economic point of view sulphadiazine is very much the cheaper drug in the treatment of bacillary dysentery.

ILIACUS MINOR

A REPORT

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and

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WHILE doing the routine work in the Anatomy Department, Medical College, Amritsar, an unusual but distinct muscular slip was found in the left lower limb of a dead body. Description of the slip is as follows :—

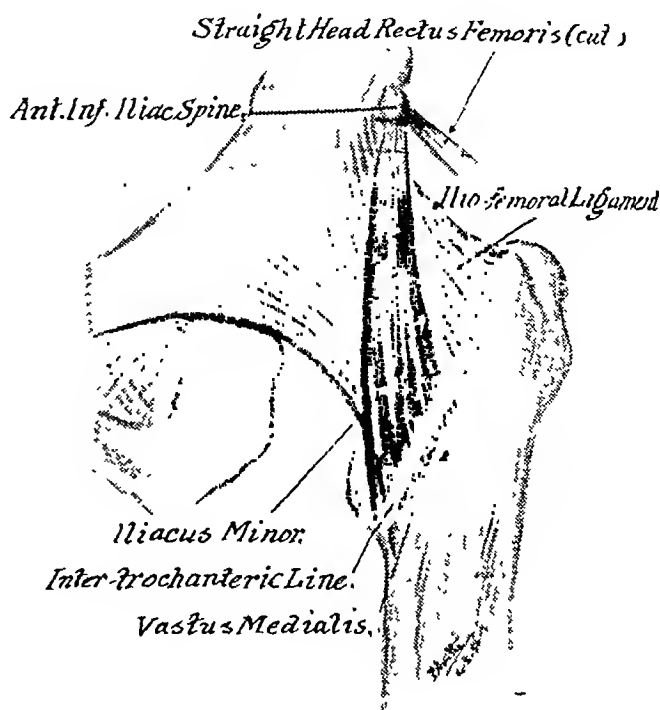
This slip of muscle took origin by tendinous fibres from the anterior inferior iliac spine, between the attachments of straight head of rectus femoris above, and ilio-femoral ligament below. From here it passed downwards deep to the ilio-psoas and in front of the capsule of hip joint. It got broadened and thinned out near its insertion into the lower part of ilio-femoral ligament and to the inter-trochanteric line just below the attachment of ilio-femoral ligament and above the origin of vastus medialis. Breadth of the muscle at its insertion was $1\frac{1}{2}$ inches (figure below).

The muscle was supplied by the nerves to the iliacus and had no separate nerve of its own.

Discussion and conclusions.—It is a very rare muscle in the human body and when present it represents a detached part of the iliacus muscle. Following two modes of insertion have been mentioned :

(a) Insertion entirely into ilio-femoral ligament (ilio-capsularis).

(b) Insertion entirely into inter-trochanteric line (iliacus minor).



Ilio-Psoas has been removed.

In this case however the muscle was inserted partly into ilio-femoral ligament and partly into inter-trochanteric line, an attachment which has not been encountered in the available literature.

This muscle corresponds to iliacus externus of lower animals.

SPONTANEOUS PNEUMO-PERITONEUM

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THE term pneumo-peritoneum is used to describe the presence of free gas in the peritoneal cavity without evident peritonitis (Leys, 1944).

Pneumo-peritoneum encountered in actual practice has been classified as of spontaneous, accidental or artificial origin (Deshmukh, 1943). Though spontaneous pneumo-peritoneum is regarded as a curiosity, d'Allaines (1932) was able to analyse 34 published cases besides one of his own. Three cases were reported by Leys and according to him spontaneous pneumo-peritoneum is not really very uncommon.

Incidentally, all the cases reported were females, except one male case reported by d'Allaines, and all were adults. The case under review is also a female. In almost all the cases reported there were symptoms referable to gastro-intestinal tract and had no evidence of pulmonary tuberculosis. The case under review

was admitted into the sanatorium for pulmonary tuberculosis and along with it had vague symptoms referable to the gastro-intestinal tract.

Case report

S. D., female, 28, was admitted on 21st July, 1949, with the complaints of rise of temperature up to 100°F., slight cough with very little expectoration, vague abdominal pain, duration eight months and amenorrhœa, duration four months.

About 8 months before admission the patient had an attack of common cold, following which she started running a temperature irregular in character varying between 99°F. and 100°F., but occasionally rising up to 101°F. Along with it she used to have slight cough, but expectoration was scanty. Later on she started getting pain in the abdomen, coming in mild attacks lasting for 2 to 3 days, during which period she used to have 2 to 3 semi-loose motions. These attacks lasted for about one month, after which she was free of her abdominal complaint for about a month, but again she started getting these abdominal attacks, till she was admitted into the sanatorium.

General examination.—The patient was slightly anæmic; otherwise no abnormal findings could be detected.

Respiratory system.—There was increased vocal fremitus with a dull percussion note both in front and back of the upper zone of the right chest. On auscultation there was bronchial breathing with a few scattered fine crepitations and increased vocal resonance in the same region. Examination of the left chest showed no abnormal findings.

Gastro-intestinal tract.—There was vague diffuse tenderness all over the abdomen without any localized rigidity. No masses were palpable, nor were liver and spleen.

Circulatory system.—Except that the patient was slightly anæmic, no abnormal findings were detected.

Examination of other systems.—No abnormality.

Skiagram of the chest was taken on 25th July, 1949, and it showed caseous pneumonic type of lesion with breaking down in the centre occupying the upper and mid-zone of the right lung field. Left lung field was clear.

Blood examination.—Hæmoglobin 75 per cent, total R.B.C. count 3,840,000 c.mm., total W.B.C. 6,875 c.mm.

Differential count (Schilling's): Neutrophils 60 per cent (stab-Kernig's 18 per cent, segmented 42 per cent), lymphocytes 33 per cent, large monocytes 5 per cent, eosinophils 2 per cent, basophils nil.

Erythrocytic sedimentation rate 32 mm. 1st hour (Westergren).

Stool examination showed a few ova of *Ankylostoma duodenale*.

Sputum examination was positive for A.F.B. on direct smear.

Artificial pneumothorax was tried on 9th August, 1949, but it was unsuccessful, following which it was decided to keep the patient on general treatment for some time more, before any major surgical treatment was adopted. Skiagram of the chest was repeated on 26th September, 1949, which showed a slight clearing of the lesion. During the course of observation the patient used to complain of pain in abdomen with slight cough and was running low grade of pyrexia with temperature varying between 99°F. and 100°F. Another routine skiagram of the chest was taken on 26th October, 1949, which showed the presence of air under the diaphragm. On questioning the patient it was found that there was neither any deterioration of her symptoms nor she was conscious of it.

On clinical examination the liver dullness was obliterated. The patient was subsequently screened on 27th October and on 31st October which confirmed the findings of the skiagram done on 26th October, by showing the presence of air under the diaphragm. The case was kept under close observation for the development of any other abnormal findings. A subsequent screen examination done on 10th November, 1949, showed that the air had been completely absorbed. During all this period the patient had no symptoms referable to her abdomen, nor was there any exaggeration of constitutional symptoms.

Barium meal examination of the gastro-intestinal tract done on 20th November, 1949, showed no abnormality of the stomach, duodenum or any part of the intestinal tract.

Stool examination still revealed ova of *Ankylostoma duodenale* for which she was given anthelmintic treatment on 24th November, 1949. Later stool examination showed no ova, etc.

Subsequent observation of the patient who is still under treatment for her pulmonary condition, clinically and by radiological examination, did not show the recurrence of the condition.

Discussion

The condition which is associated with vague and trivial symptoms has been described by Leys and others. Shoulder pain which is characteristic of artificial pneumo-peritoneum was absent in this case. Similar observations have been made out by others.

It has been thought that spontaneous pneumo-peritoneum occurs as a result of leakage of air from an ulcer of the gastro-intestinal tract and particularly of the first part of the intestine. The ulcer is so situated and is so minute as to

allow the escape of gas only without the escape of gastric or duodenal contents. Another characteristic of such an ulcer is that it heals rapidly. Exploration at laparotomy as was done in cases reported by other workers may fail to detect the perforation, which becomes sealed in the natural way in course of time and cases often recover. d'Allaines mentions the possibility of a minute perforation close to the œsophageal opening which may be inaccessible to observation even after laparotomy.

The other two possible sources of free gas in the peritoneum are :—

(1) Vaginal via the fallopian tubes.

(2) Thoracic via the diaphragmatic hiatus.

Moberg (1937) reported that vaginal douching with careless use of douching syringe may force air through the fallopian tubes into the peritoneal cavity. Another mechanism of aspiration of air along the fallopian tubes has been postulated by some workers. This is due to the result of diminished intraperitoneal pressure resulting from gastric dilatation and posture, which causes sucking in of air through the vagina via the fallopian tubes, but it has not secured the support of other workers from their study of intraperitoneal pressure.

Hinkel (1940) reported a case in which pneumo-peritoneum was thought to be due to extension of gas from the thorax to the peritoneum by way of diaphragmatic hiatus. This was thought to be due to the presence of an emphysematous bullæ demonstrated by bronchogram close to the heart.

A rare cause of intraperitoneal gas is from 'pneumatosis cystoides peritonæ' due to infection by parasites. Ova of *Ankylostoma duodenale* were demonstrated in the stools of the case under review. Pathologically, infection of the intestine due to *Ankylostoma duodenale* results in small superficial erosions or ulceration confined to the mucous membrane, but occasionally the occurrence of a minute ulceration perforating through its wall is not unlikely.

d'Allaines analysed the gas and it was found to be atmospheric and rather having high content of nitrogen. The case under review was suffering from pulmonary tuberculosis and the possibility of a tuberculous ulcer of the intestine perforating into the peritoneal cavity must be borne in mind. Perforation of tuberculous ulcer of the intestine is not uncommon and the usual seat of perforation is the ileum or the cæcum (Brown and Sampson, 1930). The cause of perforation may be mechanical due to increased pressure, which occurs, for example, just above the ileo-cæcal sphincter or above a stenosis or it may be as a result of severe acute ulcerative process. But in comparison with the large number of lesions, perforation is rather infrequent due to the following facts: (1) As the ulcer deepens the base is thickened by inflamma-

tory process and by fresh and closely aggregated tubercles. (2) Localized adhesive peritonitis occurs, matting together of loops of intestine and omentum, preventing perforation into the free peritoneal cavity. (3) Death supervenes from pulmonary tuberculosis before ulceration extends through the wall.

Summary

1. A case of spontaneous pneumo-peritoneum has been described.

2. The various ætiological factors have been discussed.

My thanks are due to Dr. T. J. Joseph, Medical Superintendent, Lady Linlithgow Sanatorium, for his kind permission for this communication and for going through the manuscript.

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BARBITURATE POISONING TREATED WITH PICROTOXIN

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THE advent of the barbiturate group of drugs as hypnotics and sedatives and their easy availability to the public has resulted in many cases of accidental or suicidal poisonings. The symptoms of such intoxication are well known. The patients are generally in deep coma with absent deep reflexes and 'extensor' plantar response. The respiration is slow and irregular and the pupils are variable in size. The pulse is rapid and weak, and the blood pressure is low.

For the treatment of this condition many drugs have been tried. Of all these, picrotoxin seems to be the drug of choice at the present moment, though claim of superiority has been put forward for other drugs.

Maloney *et al.* in 1931, after trying picrotoxin, nikethamide, strychnine, ephedrine, etc., found picrotoxin as the drug of choice. Duff and Dille in 1939 showed that picrotoxin disappeared rapidly from the blood and after two hours the quantity remaining was negligible. Blood level could be maintained only by giving injections every 15 to 30 minutes. Boyd (1946) stated that picrotoxin acted not by neutralizing the toxic effects of barbiturates but by keeping the patient alive until all or most of the depressant drug had been oxidized or eliminated from the body. Picrotoxin was given in large doses so that its convulsant effect upon the medulla oblongata would offset the depressant effect of the barbiturate and keep the patient alive till the latter had been oxidized or eliminated. For severe cases Boyd advised continuous intravenous drip of isotonic saline containing 1 mg. of picrotoxin to 1 ml. of saline the rate of administration being 1 ml. per minute for average cases. The rate should be just sufficient to keep the patient breathing deeply with good blood pressure and pulse, and in a state of slight hyperreflexia. On no account should the picrotoxin be discontinued even if convulsions occur because, if the drug is stopped, deep coma may follow and prove fatal. On the other hand if the patient begins to convulse, the dose should be cut down by reducing the rate. When the convulsions cease the rate of administration is to be increased to keep the patient in a condition as mentioned above. A useful guide to dosage is to give ample picrotoxin so that the patient will twitch slightly when pinched or tapped or needle-point applied to the skin.

Newman and Feldman (1948) reported thirty cases treated with picrotoxin. Of these, eleven cases were more or less severe ones and were reported fully or briefly. Ten of them were females. The routine treatment included provision of adequate air entry, frequent aspiration of mucus from throat, oxygen inhalation, adequate fluids intravenously, prophylactic penicillin, artificial respiration when necessary and usually gastric lavage. The chief drug used was picrotoxin, average dose being 15 mg. every 15 minutes. The total dose varied from 198 mg. to 14,196 mg., the criteria being to produce and maintain muscular twitchings just below convulsive threshold. The other drugs given were amphetamine (total dose 40 to 1,950 mg.) and desoxyephedrine hydrochloride (total dose 10 to 680 mg.). Bronchopneumonia developed in four cases in spite of prophylactic use of penicillin.

Sita-Lumsden (1949) reported a case of a man of 25 having taken 115 gr. of phenobarbitone and 150 gr. of aspirin, treated with picrotoxin in 0.3 per cent solution. The drug was given intravenously, 5 ml. *stat* and 2 ml. every 15 minutes. Atropine and penicillin were also given. On the next day the reflexes

returned and by evening there was clonic spasm. The drug was stopped for three hours and the patient relapsed into deep sleep. The drug was restarted and by the 4th day he could be easily roused. On the 5th day the drug was stopped after a total dosage of 1.65 g.

Misir (1946) treated two cases of barbiturate poisoning with picrotoxin. The first case was a young woman of 24 years, who had taken 70 gr. of soneryl; 174.5 mg. of picrotoxin was given intramuscularly in 4½ days during which the patient was unconscious. The second case, a woman of 38 years, who had taken 18 soneryl, 40 luminal and 4 nembutal capsules, was unconscious for 14 hours before treatment was started. She received 1,020 mg. picrotoxin in three days. This patient also developed pneumonia during the latter part of her unconsciousness.

Though picrotoxin has been in general use for barbiturate poisoning, claims of superiority for other drugs have been put forward by different workers. Watts and Ruthbergh (1948) thought that nikethamide was superior to picrotoxin. They said that, in contradistinction to picrotoxin, nikethamide was non-toxic and unlikely to provoke convulsions. The routine treatment advised by them was intravenous injections of 10 ml. of 25 per cent nikethamide every 5 minutes until there was return of reflexes and ability to answer questions sensibly. Supportive treatment was also given.

Freireich and Landsberg (1946) claimed the superiority of amphetamine sulphate. They stated that action of picrotoxin was less on the cerebral cortex and more on the midbrain, medulla and spinal cord with the result that the patient was in convulsion though still deeply in coma, whereas the action of amphetamine was sympathomimetic and production of wakefulness. The sympathomimetic action leads to rise of blood pressure, increase in rate and depth of respiration and increase in pulse rate. The wakefulness counteracted the soporific action of the barbiturates. Fourteen cases were treated by them with intravenous injections of amphetamine sulphate 10 mg. in 1 cc. of isotonic saline solution. Later they used 40 mg. and continued with 20 mg. every 30 minutes. Supportive treatment as required was also given. The barbiturate taken in these cases varied from 12 gr. to 60 gr. and amphetamine required was from 40 mg. to 400 mg. Blood pressure and pulse rate were seen before each injection. The pupils became dilated and remained so during the course of treatment. Even when as high a dose as 400 mg. was given no unusual toxic effects were observed.

Case reports

The following cases were admitted in the Medical College Hospitals under one of us (N. R. K.):—

Case 1.—G. B., a female, aged 22 years, was admitted at 8-30 a.m. on 8th March, 1950, with history of taking 23 luminal tablets of gr. $1\frac{1}{2}$ each on 7th March at about 10 p.m. She was not in the habit of taking hypnotics. She was unconscious and restless. Pupils were moderately contracted and reacted sluggishly to light. Neck was soft. Kernig's sign was negative. Deep reflexes were sluggish. Abdominal reflex was absent. Plantar reflex gave 'extensor' response on both sides. No abnormalities were detected in heart, lungs or abdomen. Blood pressure 110/85 mm. of Hg., temperature 98°F., pulse 110 and respiration 22 per minute.

On admission the stomach was washed out with warm water and she had an intravenous injection of 4 ml. of 0.3 per cent solution of picrotoxin. She was later put on intravenous injections of 2 ml. picrotoxin at an hourly interval and coramine 2 ml. intramuscularly every four hours. In the evening of 8th March she was put on subcutaneous injections of strychnine gr. 1/60 every 8 hours, and picrotoxin was given in doses of 2 ml. intramuscularly every 4 hours. The bowel was washed with warm water. On 9th March penicillin was started in doses of 50,000 units intramuscularly every 6 hours as a prophylactic measure against pulmonary complications. On that day she became fully conscious and picrotoxin was omitted. Injection of strychnine was stopped on 10th March, coramine on 11th March and penicillin on 13th March. On the day of admission the temperature went up to 100°F., otherwise she was afebrile till 14th March. Blood: White blood cells 12,900 per c.mm., polymorphonuclears 78 per cent, lymphocytes 20 per cent, monocytes 1 per cent, and eosinophils 1 per cent. Urine contained barbiturate.

On 15th March the electrocardiogram did not show any abnormality. On 14th March the temperature had gone up to 100°F. and she had developed a morbilliform rash all over the body. She complained of headache and aches and pain over the limbs. There was no coryza. This irregular fever, varying from 98°F. to 101°F., persisted from 14th March to 20th March during which she had penicillin 50,000 units every 6 hours. She left the hospital on 21st March, 1950, when she was completely afebrile.

Case 2.—V. T., a married Indian female, aged 27 years, was admitted at 11-50 a.m. on 2nd April, 1950, with history of taking a few tablets of soneryl (butobarbitone). The patient had been suffering from insomnia for the previous 5 months for which she was in the habit of taking hypnotics. On 1st April at about 9 p.m. she took 2 tablets of soneryl. She was however awake at 2 a.m. of 2nd April when she took a few more tablets, the exact number of which she could not recollect. At 8-30 a.m. she was found lying unconscious on the floor.

At 11-30 a.m., the patient was unconscious, and markedly restless. She had to be restrained on the cot. Temperature 97°F., pulse 104 and respiration 26 per minute. Blood pressure 130/70 mm. of Hg. Pupils were moderately dilated and reacted sluggishly to light. Deep reflexes were sluggish. Plantar reflexes gave 'extensor' response. Neck was soft and Kernig's sign negative. Blood: White blood cells 8,000 per c.mm., polymorphonuclear cells 68 per cent, lymphocytes 25 per cent, monocytes 4 per cent, eosinophils 3 per cent. Urine, stool and cerebrospinal fluid were normal.

In the emergency room she had intravenous injections of 2 ml. coramine and 3 ml. of 0.3 per cent picrotoxin. The stomach was washed with plain water. On transfer to the ward she was put on intramuscular injections of coramine 2 ml. every 4 hours and strychnine gr. 1/60 every 8 hours. Picrotoxin was injected intravenously 2 ml. of 0.3 per cent solution every half hour till the patient became just conscious. In the afternoon a bowel wash was given and the bladder was evacuated by a catheter. She was markedly restless. The picrotoxin and strychnine were omitted. Penicillin was injected intramuscularly in doses of 50,000 units every 6 hours. At 10 p.m. she was so boisterous that 8 ml. of paraldehyde was injected intramuscularly, which made her quiet. The coramine was omitted on the 4th and penicillin on the 5th April. For the first three days in hospital she had irregular temperature varying from 99°F. to 100°F.

Case 3.—R. L. B., an Anglo-Indian male, aged 25 years, was admitted on 19th April, 1950. He was said to have taken 10 tablets of sedormid (allyl-isopropyl-acetyl-carbamide) on 18th April at 8 p.m. and was brought unconscious to the hospital on 19th April at 2 p.m. The patient was in the habit of taking the drug for insomnia. On admission he was in deep coma. Corneal reflex was absent. Pupils were slightly contracted and did not react to light. Neck was soft and Kernig's sign negative. Deep reflexes were absent. Plantar reflex gave bilateral 'extensor' response. Râles were heard all over both the lungs. Temperature was 104°F., pulse 140 and respiration 56 per minute. Blood: White blood cells 12,000 per c.mm., polymorphonuclear cells 80 per cent, lymphocytes 20 per cent, monocytes nil, eosinophils nil. Urine, stool and cerebrospinal fluid were normal.

On arrival in the hospital the stomach was washed with plain water. He was put on intravenous injections of picrotoxin at 15 minutes interval. The dose was gradually increased from 2 ml. to 5 ml. In the morning the unconsciousness was less deep and the dose of picrotoxin was reduced to 2 ml. It was given intramuscularly every half hour. On the evening of 21st April the dose was further reduced to 1 ml. given intramuscularly every

hour. The drug was omitted on 23rd April. The amount of picrotoxin given on each of the four successive days from 19th April was 36 ml., 50 ml., 24 ml. and 24 ml. He also had coramine 2 ml. intramuscularly every 4 hours from 19th April to 23rd April. Penicillin was injected intramuscularly in the dose of 50,000 units every 3 hours from 19th April to 26th April.

On 20th April, 1950, the patient was unconscious. The limbs were flaccid and the deep reflexes were absent. Plantar reflex gave flexor response. Temperature varied from 99.5°F. to 102°F. Respiration was 48 per minute and scattered râles were present over both lungs.

On 21st April, 1950, patient was semiconscious. Pupils were normal in size and reacted well to light. Deep reflexes returned but were sluggish. Temperature 99°F., pulse 90 and respiration 30 per minute.

On 22nd April, 1950, patient was conscious. A few rhonchi were heard over both lungs. Pupils and deep reflexes were normal. The temperature gradually settled on 30th April. A gastric drip had been set up during the period the patient was unconscious to maintain nutrition and hydration. A skiagram of the chest was taken on 25th April, which did not show any abnormality. The patient left the hospital on 1st May, 1950.

Case 4.—S. T., a married Indian female, aged 23 years, was admitted on 20th April, 1950, at 3 a.m. with history of taking a few tablets of sonalgin (each tablet contains butobarbitone gr. 1, codeine phosphate gr. 1/6, phenacetin gr. 3½). On admission she was in deep coma. Pupils were contracted and did not react to light. Limbs were flaccid. All superficial and deep reflexes were absent. Temperature 98°F., pulse 120 and respiration 20 per minute. Blood pressure 80/60 mm. of Hg. No abnormality was detected in the heart, lungs or abdomen.

On admission the patient had a stomach wash. Later she had a bowel wash with warm water and the bladder was evacuated by a catheter. The urine contained barbiturate. Nutrition and hydration were maintained by gastric drip feeds. Penicillin was given in doses of 50,000 units 6 hourly. She had coramine and strychnine but main reliance was placed on picrotoxin. The drugs were given in the following doses:—

20th April, 1950. Day: Picrotoxin 3 ml. intravenously every 15 minutes. Total 60 ml. Coramine 2 ml. intramuscularly 4 hourly. Strychnine hydrochlor gr. 1/60 every half hour 6 injections.

Night: Picrotoxin 4 ml. intramuscularly every half hour. Total 96 ml. Coramine 2 ml. intramuscularly 4 hourly.

21st April, 1950. Day: Picrotoxin 2 ml. intramuscularly every hour. Total 24 ml. Coramine 2 ml. intramuscularly 6 hourly.

Night: Picrotoxin 2 ml. intramuscularly 2 hourly. Total 12 ml. Coramine 2 ml. intramuscularly 6 hourly.

22nd April, 1950: Picrotoxin 2 ml. intramuscularly 4 hourly 2 injections only: 4 ml. Total amount of picrotoxin used was 196 ml.

The patient became conscious and took her feeds well. Pupils were normal and reacted well to light. Deep reflexes were still absent, plantar reflex gave 'flexor' response.

On 25th April, 1950, the patient was quite well and the tendon reflexes returned.

The patient ran irregular temperature varying between 99°F. and 100°F. from 20th April, 1950 to 29th April, 1950.

Discussion

With greater use of sedatives and hypnotics, poisoning by barbiturate group of drugs is not an infrequent incident. Four cases were admitted in one of the wards of the Medical College Hospitals during one month. All the patients were young adults and except one they came from upper economic strata of the society. Three were females and one male. The amount of drug taken in each case was not definitely known. The drugs used in the different cases were luminal, soneryl, sedormid and sonalgin. All the patients were in deep coma during admission. Pupils were variable in size. During return of consciousness one talked incoherently and one was restless and obstinate. The other two patients did not show any peculiarity. The patients ran irregular temperature for periods varying from 3 to 10 days. The patient who took luminal developed a morbilliform rash a week after the incident. On arrival at the hospital the patients had a stomach wash. Bowel wash was given later on. Nutrition was maintained by nasal feeding during periods of unconsciousness. Retention of urine was relieved by catheterization. Penicillin was used as a prophylactic against pulmonary complications. Oxygen was given when needed. Coramine and strychnine were used but main reliance was placed on picrotoxin. Total amounts of picrotoxin used in different cases were 32 ml., 15 ml., 134 ml. and 196 ml. of 0.3 per cent solution.

Summary

Four cases of barbiturate poisoning have been described. All of them recovered.

Picrotoxin was found to be an effective antidote.

All the patients ran irregular temperature for periods varying from 3 to 10 days. Three of them had the temperature from the day of poisoning, the other one developed temperature and morbilliform rash a week after taking the drug. Pupillary changes were inconstant.

We are grateful to Dr. D. C. Chakraborty, Superintendent, Medical College Hospitals, Calcutta,

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ARGEMONE AND MUSTARD SEEDS

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THERE is at present considerable agitation in the country over the adulteration of mustard oil with argemone oil. It has been fully realized that ingestion of mustard oil contaminated with argemone oil produces symptoms similar to those of epidemic dropsy. The experiments carried out in the field and the observations made by the various workers in this respect support the argemone contamination theory in the causation of epidemic dropsy. A few of these names may be mentioned, e.g. Lal, Chopra, Chaudhuri, Sarkar, etc. The credit for the idea underlying this theory should however be given to Dr. Sarasi Lal Sarkar (1926). At that time there were two divergent views which held the field: one was that the disease was due to contaminated rice and the other to deficiency in diet.

It is true that the disease has been noticed mostly among the rice-eating population but it has not been possible to produce the disease by feeding on contaminated rice. As some of the symptoms in epidemic dropsy are similar to those noticed in beri-beri, the two diseases were at one time thought to be of common origin. Detailed investigations subsequently led to the conclusion that the two were different and that the ætiological backgrounds were also different.

While it has been held that the toxic principles of argemone seeds gain entrance into the system through the alimentary canal, there are undoubtedly a certain number of cases of epidemic dropsy where no mustard oil has been taken with food. The writer came across a few

such cases at Banaras at the time when the great epidemic swept practically over the whole of Bengal during 1934 to 1939. At Banaras, eye symptoms, especially glaucoma, were a particular feature of the disease. The fact that patients who are not in the habit of taking mustard oil yet suffer has been explained to be due to contaminated mustard oil being used for anointing the body before bathing.

Epidemic dropsy has assumed a serious public health problem at least in certain parts of India where mustard oil is consumed. It has been taken for granted that the contamination of mustard oil with argemone oil is merely accidental as it is widely believed that both mustard and argemone often grow in the same field and at the same time and that the harvesting of both is done also simultaneously. The farmer is said not to pay much attention to the separation of one from the other at the time of harvesting as it is believed that argemone seeds are oil-producing and at the same time harmless.

To a common observer both argemone and mustard seeds look almost alike and unless critically examined the difference is difficult to detect. As the argemone seeds are of dark colour, they get mixed up with the black mustard. Sometimes white mustard is also mixed with black mustard in which there may be a small fraction of argemone seeds. The contamination is seldom found in a high proportion and the presence of a few argemone seeds in a sample of mustard strengthens the view in favour of accidental mixture.

If it is remembered that an argemone seed on account of its hard testa will burst with a report when pressed with the nail of the thumb, while a mustard seed, being much softer, will burst easily without any appreciable sound, the detection of the difference will be easy.

The author in order to determine whether the presence of argemone in mustard is accidental or deliberate made extensive investigations in the field and came to the conclusion that the presence of even 'a few' grains of argemone must be regarded as deliberate. When we take into consideration the relative oil-producing properties of the two, we find that argemone seeds will yield a higher proportion of oil than mustard. Generally speaking mustard seeds will yield 30 to 33 per cent of oil whereas argemone will yield as much as 36 per cent. There is a gulf of difference between the prices of the two seeds: while mustard seeds are sold at Rs. 36 per maund, argemone seeds are obtainable at Rs. 5 and therefore a mixed oil will be cheaper than pure mustard oil.

The argemone grows wild especially in barren fields and waste lands. It is never cultivated and there is no harvesting in the sense used for other field produce. Mustard is sown after the rains in October and is harvested before spring

from January to February. Argemone capsules on the other hand will not mature before late summer, i.e. May. A few argemone plants may occasionally grow along with mustard in the same field. The former are as a rule cut down and on account of the thorny nature of the plants, they are never collected with the mustard but are thrown away at the time the harvesting of mustard is done.

The argemone plant is different in every respect from the mustard plant. Although the sprouting of the former takes place in the cold season, yet the flowers do not appear before February. The capsules appear from March onwards and the seeds lie within the capsule. The latter, when dry, burst at the top but the seeds do not escape until the capsules, which yet remain attached to the plant, point downwards. The seeds are ultimately scattered on the ground. There is never any real showing of argemone. On account of the thorny nature of the plant, including its leaves and capsules, it is difficult to handle either the whole or any part of the plant. For the collection of the seeds, a small basket is held underneath the dried plants which are beaten by means of a stick. The capsules are hit and the seeds which lie loose in the capsule fall into the basket.

The capsule of *Argemone mexicana* is about 1 to 1½ inches long, more or less oval in shape, intensely prickly and opens by valves at the apex.

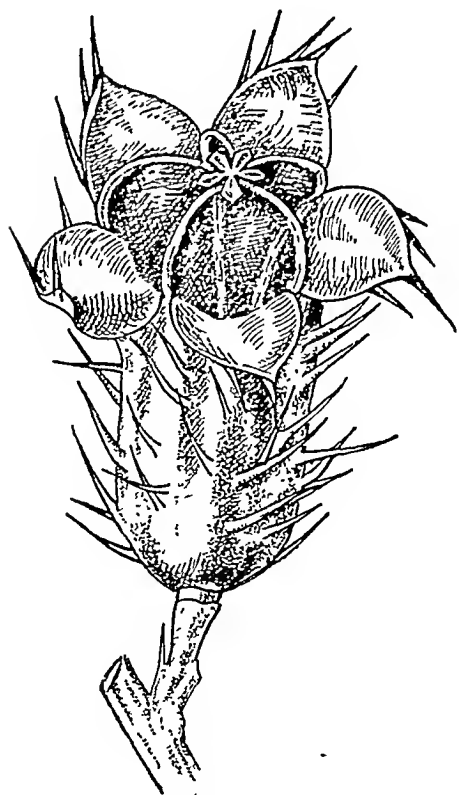


Fig. 3.

Figures 1, 2 and 5 (plate L) and figures 3 and 4 (a and b) below will show the character of the plants, capsules and seeds of argemone plants and also of mustard seed.

In the countryside it is not unusual to find waste fields in which there are heavy growths of argemone plants. This creates the impression that the plant has been purposely cultivated for its seeds. This is an erroneous idea. The fields are waste lands and the seeds which drop to the ground lie dormant till the next sprouting season. In this way heavy growths of argemone plants in a field take place.

Figures 6 to 8 (plate L) show various argemone fields.

The moot point therefore is to determine whether the occasional presence of a few grains of argemone with mustard should be regarded as wilful or accidental adulteration. Taking all things into consideration, particularly the time of ripening of argemone seeds, which takes place in late summer when mustard has already been collected and stored away, its good yield of oil, its ridiculously low price in comparison to the price of mustard and its easy availability, the general opinion would be in favour of wilful adulteration.

The commercial people hold that the presence of argemone seeds in mustard is not adulteration but is merely accidental and in support of the latter contention it is argued that otherwise a much higher percentage of argemone would be found. However, recently cases have been brought to light in the Punjab where fatal consequences have resulted after taking mustard oil very highly adulterated with argemone oil, death having taken place within two to three days. In the ordinary course it is generally a slow poison due to the cumulative effects of the toxic principles of argemone.

There is now a tendency on the part of the health authorities to devise means to neutralize the toxic effects of argemone. Studies are being carried out in this line in different places



Fig. 4a.

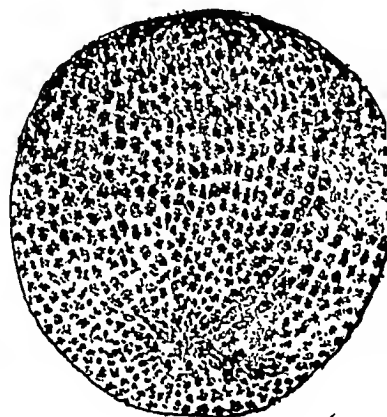


Fig. 4b.

in India. While it is no doubt easy to detoxicate a contaminated sample of mustard oil, it is difficult to retain all its essential properties which are valued so highly for being used for cooking purpose.

The writer is convinced that argemone is used as an adulterant of mustard, its presence in a sample of mustard does not indicate an accidental event, and that the presence of an appreciable amount of argemone in mustard oil must be regarded as wilful and should be stopped by law. The detoxication should not be enough : the oil should be made unfit for human consumption by denaturing (like methylated spirit) and used up for some other purpose (illumination, soap-making, lubrication, etc.).

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EXPLANATION OF FIGURES

Fig. 1.—*Argemone mexicana* Linn. showing immature capsules. The leaf, stem and the capsule are spinous. The plant was collected in May 1950.

Fig. 2.—Shows well-grown plants of *A. mexicana* Linn. with immature capsules and still in the flowering stage. All parts of the plant except the petals of flowers are spinous. Prominent veins are seen in the back of the leaf which are spinous. This plant was collected in the first week of May.

Fig. 3.—Shows a mature capsule of *Argemone mexicana* Linn. which has opened at the top.

Fig. 4a.—Shows a magnified view of an argemone seed. The seed is nearly spherical, bears a stalk attached to the upper end; the surface is rough with ridges and depressions. The testa is hard and brittle, when pressed with the nail of the thumb bursts with a report.

Fig. 4b.—Shows a magnified view of a mustard seed. The seed is nearly spherical, the surface appears smooth but when seen under magnification fine ridges are seen on the outer surface; it is soft and when pressed with nail of the thumb bursts without any appreciable sound.

Fig. 5.—The mustard pods and the argemone capsule are placed side by side.

Fig. 5a.—Mustard pods were collected from Bengal in the end of January.

Fig. 5b.—Almost matured argemone capsules.

Fig. 5c.—Mustard pods collected from U.P.

Fig. 6.—Shows a large argemone field in the flowering stage. Photograph taken in the end of April.

Fig. 7.—Shows a group of road-side plants of argemone still in flower. Photograph taken in Orissa in the middle of May.

Fig. 8.—Shows a large argemone field grown on waste land. Plants mostly containing immature capsules. Photograph taken about the end of May.

STUDIES ON PLASMA PROTEIN

III. MALARIA

By H. CHAKRAVARTI, M.D. (Cal.)

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Two distinct groups of cases were encountered during the study of plasma proteins in malarial patients. One was acute malaria, which showed all the features of an acute febrile infection. The other was chronic relapsing malaria, some cases were inadequately treated, and many had : hepatomegaly and splenomegaly.

Plasma proteins of 40 patients, admitted in the hospital, were studied and in all of them malaria parasite was found in the peripheral blood. Out of these cases 9 had acute malaria, who gave no history of malarial infection at least in the recent past. Plasma proteins were determined within 7 days of the onset of the disease, during febrile period without any relation to the rigor and before any treatment was given. In the other group of 31 patients, the history of the disease was quite different. They were admitted in the hospital for fever but the attacks were neither primary nor acute. They had been suffering from malarial fever for a varying period, extending over years in some cases.

Distributions of plasma proteins and their fractions are graphically represented in figure 1.

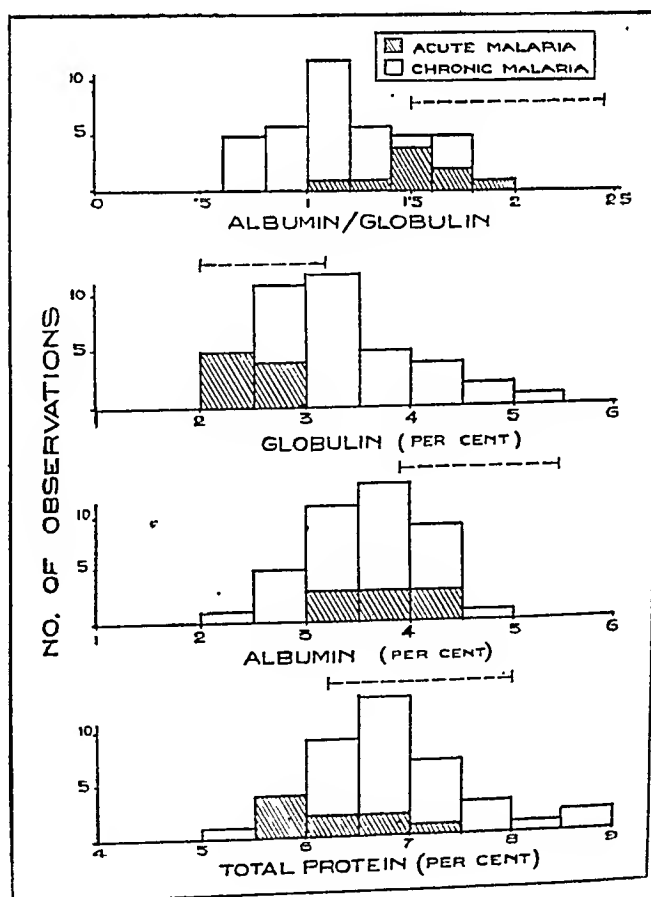


Fig. 1.

A. *Acute malaria*.—There were 3 cases of *P. falciparum* and 6 cases of *P. vivax* infection. No noticeable difference was observed between these two groups. In general, there was no remarkable variation in plasma proteins in acute malaria. Total protein, albumin fraction and A/G ratio are somewhat lowered than the normal values, globulin being within normal range in all.

TABLE I

Showing plasma proteins in acute malaria (9 cases)

	Total protein	Albumin	Globulin	A/G X : 1
	(gm. per cent)			
Range ..	5.8-7.2	3.1-4.5	2.3-2.9	1.1-2.0
Arithmetic mean.	6.3	3.7	2.6	1.5

Total protein.—This was normal in 3 cases and in 5 cases it was below the normal limit.

Albumin.—In 3 cases within normal limits and in 5 cases below it.

Globulin.—All within normal limits.

A/G.—In 6 cases within and in 3 cases below the normal limit. Normal levels observed in 3 cases were examined within 3 days of the disease. In others, the disease was of more than 3 days' duration.

The slight reductions of total protein observed in these cases are at the expense of the albumin fraction.

B. *Chronic (relapsing) malaria*.—This group comprises 31 patients. In all of them there was history of similar attacks in the recent past. In 27 *P. vivax* and in 3 *P. falciparum* and in 1 *P. malariae* were found in the blood. It was however difficult to group them according to the duration or chronicity of the disease, as in most cases actual duration of the disease could not be ascertained correctly; moreover, the result of the previous treatment, an uncertain factor, must be borne in mind. They have been classified according to the size of the spleen. Although enlargement of the spleen in these cases cannot be regarded as an index of the duration of the illness nor of the chronicity, yet it was the only practicable method under the circumstances.

Group I—No enlargement of spleen (not palpable) .. 9 cases

Group II—Spleen just enlarged (palpable) .. 6 cases

Group III—Spleen enlarged up to 2 inches below costal margin .. 8 cases

Group IV—Spleen enlarged more than 2 inches below costal margin .. 8 cases

Range and mean values and standard deviation of plasma protein levels including their fractions in these groups are tabulated below (table II) and they are graphically represented in figure 2.

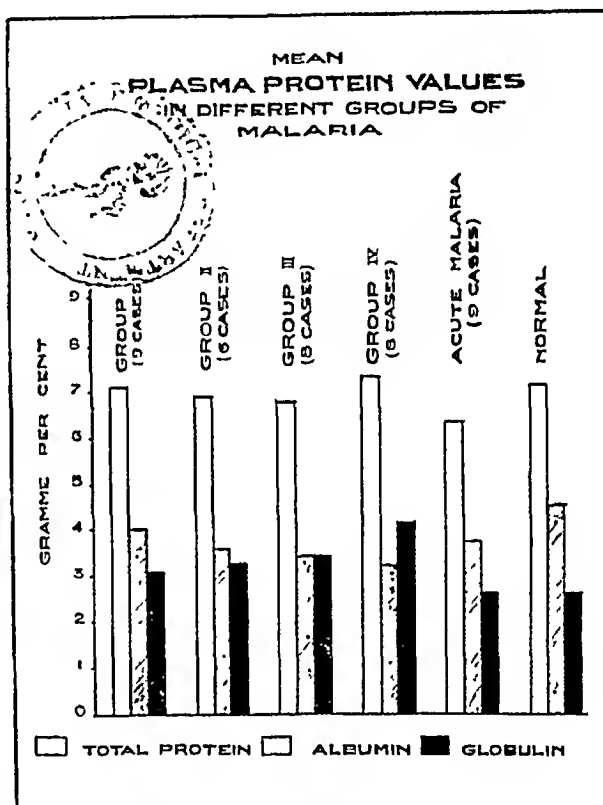


Fig. 2.

It will be evident from table II that there is much individual variation in each group but there is a group characteristic feature in each of them which justifies the classification of these cases according to the splenic enlargement. Total protein is more or less same in all the four groups but albumin begins to fall along with the degree of the enlargement of spleen while globulin rises directly with the splenic enlargement. Albumin/globulin tends to be lower like albumin fraction, but the variation is not only due to lowered albumin but also due to increased globulin.

Taking all the cases together, total protein remained within normal limits in 25 cases (80 per cent), in 3 cases (10 per cent) it was low and in 3 cases (10 per cent) it was

TABLE II

			Total protein	Albumin	Globulin	A/G X:1
			(gm. per cent)			
Group I (9 cases)	...	Range ..	6.5-7.9	3.5-4.6	2.4-3.7	1.1-1.7
		Mean ..	7.1	4.0	3.1	1.3
		S.D. ± ..	0.35	0.33	0.37	0.24
Group II (6 cases)	..	Range ..	6.5-7.2	3.3-3.9	3.0-3.8	0.9-1.3
		Mean ..	6.9	3.6	3.3	1.1
		S.D. ± ..	0.39	0.32	0.22	0.32
Group III (8 cases)	..	Range ..	6.1-8.2	3.0-4.4	3.0-3.9	0.7-1.2
		Mean ..	6.8	3.4	3.4	1.0
		S.D. ± ..	0.53	0.49	0.33	0.14
Group IV (8 cases)	..	Range ..	5.0-8.8	2.0-4.3	3.0-5.6	0.6-1.0
		Mean ..	7.05	3.15	3.9	0.8
		S.D. ± ..	1.23	0.66	0.78	0.14

above this level. Albumin was below the normal range in 23 cases (74 per cent) and globulin was higher in 18 cases (58 per cent). Although total protein was within normal limits, in many cases albumin/globulin ratio was markedly changed, in 28 cases (90 per cent) being lower than the normal range.

Unfortunately not many cases were followed up after the antimalarial treatment. In only 3 cases, one acute and two chronic, plasma proteins were examined again, more than a month after the institution of the treatment. These patients were kept in the hospital to study the effect of new synthetic antimalarial drugs. These three observations are given in table III below:—

Lloyd and Paul (1929) observed depression of total albumin fraction and relative rise of globulin. Similar observations were made by Chopra *et al.* in 1935, who studied plasma proteins of malarial patients during and after rigor. However, their studies were done probably on acute malarial patients (as no reference was made regarding the duration of the illness). Very little work is available regarding the plasma protein changes in chronic relapsing malaria. Ghosh and Sinton (1935) studied plasma protein changes in monkeys and found similar results. They concluded that the changes of plasma proteins were not specific and were correlated with the intensity of the infection in the monkey. In the interval between

TABLE III

Types of cases			Total	Albumin	Globulin	A/G	Spleen
Acute malaria	Before ..		6.0	3.6	2.4	1.5	Palpable.
	After ..		7.1	4.3	2.8	1.5	Not palpable.
Chronic relapsing group II ..	Before ..		6.8	3.2	3.6	0.9	2 inches.
	After ..		6.5	3.4	3.1	1.1	$\frac{1}{2}$ inch.
Chronic relapsing group IV ..	Before ..		7.0	3.6	3.4	1.1	Not palpable.
	After ..		7.2	4.0	3.2	1.25	Do.

The number of cases is too small to comment on this subject. But the present writer is of opinion that in acute malaria, as expected, restoration of plasma protein level to normal limit is easy and possible soon after the treatment. But in chronic malaria where damage has been done to liver and spleen for sometime, correction of plasma protein abnormalities must take time and it may not follow the clinical improvement after the treatment.

Discussion

Studies in plasma protein changes in malarial patients were done by some workers in the past.

relapses the plasma protein tended to return to normal, an improvement that was accentuated by treatment. Later observations on human subjects have also agreed with those findings (Boyd and Proske, 1941; Kopp and Solomon, 1941).

Dole and Emerson (1945) while studying electrophoretic pattern of malarial plasma found normal protein concentration in 8 relapsing *vivax* malaria but depression of albumin and increase in globulin fraction notably fibrinogen. But in one severe *falciparum* infection, extreme depression of total protein at the expense of the albumin fraction was observed.

In the present study, changes observed in acute malaria are not much significant and such changes as have been observed, are apt to occur in any febrile disease. Moreover, the degree of the changes—lowered total protein at the expense of albumin—is pronounced as the disease progresses, probably due to increased catabolism which exhausts the protein reserve and affects the plasma protein finally. More depression is expected in more severe cases and thus, as Dole and Emerson have suggested, measurement of total protein and changes of A/G ratio may aid in evaluating the severity of the case.

In the chronic relapsing group, which is probably the largest of its kind ever studied, the results are somewhat different. Reference has already been made to the work on monkey by Ghosh and Sinton (loc. cit.) who were of opinion that the plasma protein change, depression of albumin and rise in globulin tended to return to normal in the interval between relapses. Dole and Emerson also found, in two of their cases followed by repeated examination, similar results. They opined that changes observed in relapsing *vivax* infection were in the nature of 'host reaction' rather than what is observed due to the infection. Changes observed by the present writer were so characteristic of chronic infection that in all probabilities at least part of the changes must be regarded as a result of chronic malarial infection and in most cases it was proportionate to the enlargement of the spleen. It must also be noted here that one of the effects of chronic malarial infection in these cases was depression of liver function which in turn might give rise to lowering of albumin and increase in globulin fraction of the plasma.

Rise in the globulin fraction of plasma in chronic malaria cases may be the cause of positive antimony (Chopra's) test and formolgel reaction in many of them. But changes of plasma proteins observed in these cases are never so pronounced as in kala-azar when compared with similar group of cases according to the splenic enlargement, and this observation may act as a point of differentiation between these two chronic parasitic infections.

Summary

Plasma proteins of 9 acute malaria cases and 31 chronic relapsing cases were estimated.

1. In the acute malaria cases there was slight reduction of the total protein at the expense of the albumin fraction. More depression of albumin fraction is expected in severe cases but the changes are like those in many other acute febrile conditions.

2. In the chronic relapsing group albumin fraction was more depressed, globulin was raised and the total protein remained more or less normal. Changes were more pronounced in chronic cases and there seems to be a correla-

tion between such changes observed and splenic enlargement. However, they were not so marked as in kala-azar.

3. The present observations have been compared with the findings of the other workers in this field.

My grateful thanks are to Professor R. N. Chaudhuri under whose guidance this work was done.

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A Mirror of Hospital Practice

AUREOMYCIN IN THE TREATMENT OF PEMPHIGUS FOLIACEUS

A CASE REPORT

By D. PANJA

J. C. GUPTA

and

A. K. BANERJI

(School of Tropical Medicine)

K. C. B., a male, aged 56 years, came to the Carmichael Hospital for Tropical Diseases on the 8th August, 1950, with the following complaints:—

Patient was highly toxæmic, the condition was grave and alarming, temperature 103°F., pulse 120, respiration 28 per minute. There was generalized œdema with exfoliative dermatitis all over the body including face and head.

Ulcers of various sizes were also present on chest, back and extremities. There were a few small flaccid blisters on the chin containing a faint yellowish coloured fluid. Regarding exfoliation the scales were thin and big and were easily removable by a gentle manipulation, leaving a moist raw surface which was covered with foetid gummy exudate (figures 1 and 2, plate LI). The unpleasant foetid smell of this exudate was so objectionable that the patient had to be isolated from other patients. The subjective symptom of pain was very little but the itching was very prominent so much so that the patient complained of sleepless nights. Both the eyes were affected with conjunctivitis; purulent discharge and photophobia were present, pain was negligible and the cornea was not affected. The head was fully matted with yellowish moist scales, with scanty hairs. Mucous membrane of

the mouth was not affected and the nutrition was well maintained. A mild diarrhoea, with 2 to 3 loose stools a day, was present and the urine was scanty.

Past history.—On the 7th May last, *i.e.* three months back before he came into the hospital, the patient noticed a tiny blister on the pinna of his left ear and after a week a small crop of flat blisters appeared on the left side of the face. The blisters remained for a fortnight: some ruptured, leaving a raw red base and some formed crust with sticky exudate underneath. In the first week of June fresh crops of flat bullæ containing a yellowish fluid appeared symmetrically on both ankles. The ear and face lesions were gradually disappearing but the bullous eruptions of ankles extended to the knees within a few days. These blisters were multi-form, some entire with fluid inside, some ruptured with raw red surface denuded of epithelial covering and some with scales which were easily removable by gentle manipulation. The same sort of blisters then appeared on the chest after a fortnight. During this period the subjective symptom of pain was negligible except the trouble of itching, specially at night. He took some homœopathic treatment for some time with the result that the blisters gradually dried up within a few days but very soon came out again more vigorously involving the whole of the body including the face. The blisters were multi-form and flat with faint yellowish fluid inside; they used to rupture easily on gentle pressure and after some time were replaced by a generalized exfoliative dermatitis, with a very foetid serous exudate underneath the scales. The scales were thin, leaf-like and moist. From the first week of July he developed temperature ranging from 99°F. to 101°F., diarrhoea, general weakness, sleeplessness and debility. He gave up homœopathic treatment and took the following treatment outside: 4,000,000 units of penicillin in '10 days' time, arsenic orally, diuretic mixture and various local applications. There was no improvement regarding the skin condition except that penicillin controlled the rise of temperature for a few days. The treatment was continued up to 3rd August. The temperature began to rise again, a few blisters appeared here and there, more on face, and he came to the hospital on 8th August, 1950.

Laboratory findings

Blood.—Total erythrocyte count ranged from 3 to 4 millions, leucocyte count was 7 to 10 thousand with a differential count of 70 to 80 per cent neutrophil, 8 to 15 per cent lymphocyte, 2 to 5 per cent monocyte and 2 to 5 per cent eosinophil. Hæmoglobin content 10.5 gm. to 14.5 gm. Van den Bergh test, direct and indirect, both negative. Sedimentation rate was within normal limits. Serologic tests for syphilis were negative. Blood chemistry was normal. Malaria parasite and microfilæria were

negative on repeated examinations.

Urine was normal. ■

Stool did not show any protozoa, helminth or any non-lactose fermenting organism on repeated examinations.

Treatment while in the hospital

Local.—Condy's and Bran bath once a day, liniment calamine, olive oil, 2 per cent boric ointment and 2 per cent hydrargyri ammoniata ointment.

Internal.—Orally alkaline mixture with salicylate, vitamins C and K, yeast tablets, sulphadiazine, laxatives off and on and parenterally glucose, calcium, vitamin C and liver extract.

The above treatment was continued for a fortnight without any improvement. On the contrary the condition became grave with remittent temperature ranging from 101°F. to 103°F., loose motion, weakness and extreme debility. Skin condition was also very bad with foetid, unpleasant smell. Then we started aureomycin on 22nd August, 1950, according to the report of Bettley (1950), 250 mg. per dose being given 5 times daily. Within 4 days the skin condition started getting better, there was morning remission of temperature. After 10 days there was dramatic improvement. Skin cleared up of its blisters and exfoliative condition, temperature became normal and diarrhoea stopped. Eyes were free from conjunctivitis and purulent discharge, and the general condition of the patient was markedly improved. 4 gm. more were administered and by the 13th September the patient could sit on his bed with negligible exfoliation on the skin here and there and no temperature. We noticed a few fresh blisters again after the stoppage of aureomycin which was started again in the dose of 250 mg. 3 times a day and the blisters disappeared within 2 days (figures 3 and 4, plate LI).

Comment.—The patient had the routine treatment of pemphigus with arsenic, sulphadiazine, etc., in addition to various local applications for symptomatic relief. 40 lacs of penicillin were administered with no appreciable benefit except that it controlled the temperature for a few days. Aureomycin acted more or less dramatically, clearing up the lesions within a few days and the patient's general condition improved rapidly. There are often long spontaneous remissions in the course of the disease and it will not be fair to claim the recovery from the administration of aureomycin so soon and we will keep the patient under observation. The patient was really in a grave condition and the prompt and dramatic improvement immediately after the administration of aureomycin tempted us to report this case as to the efficacy of the antibiotic which should also be tried by other physicians.

REFERENCE

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Fig. 1.



Fig. 2.



Fig. 5a.

Fig. 5b.

Fig. 5c.



Fig. 6.

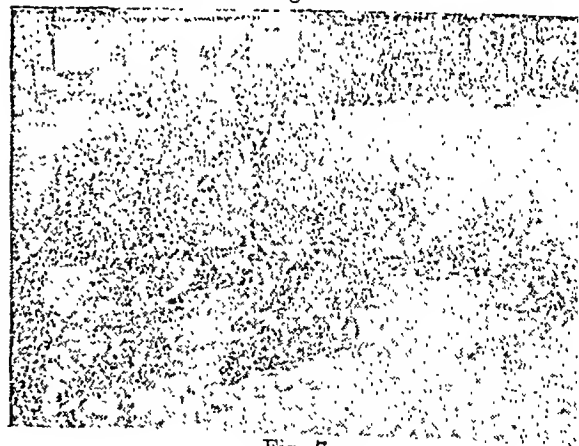


Fig. 7.





Fig. 1.

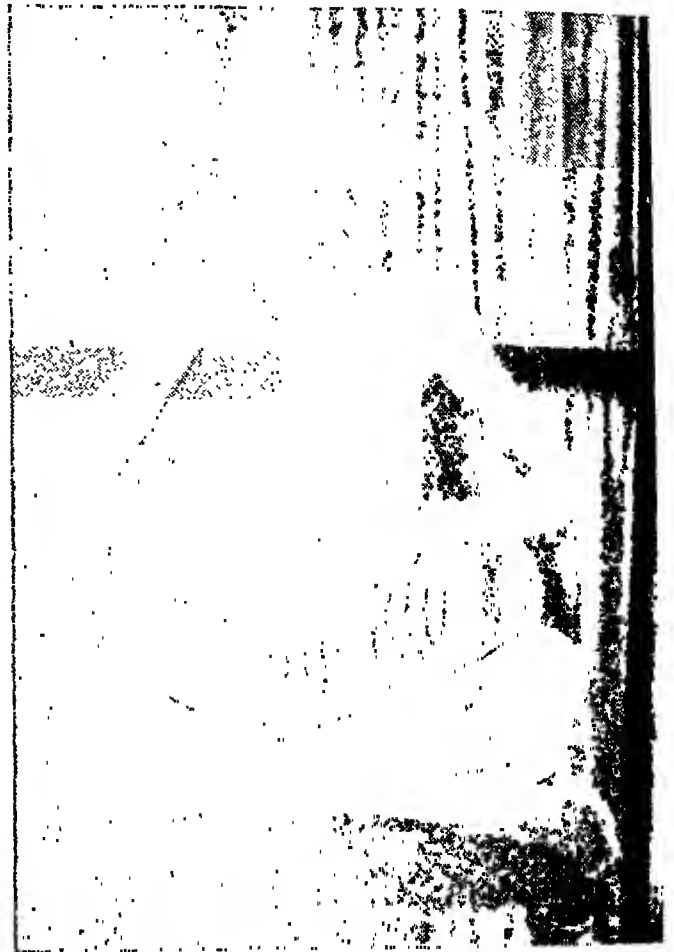


Fig. 3.



Indian Medical Gazette

NOVEMBER

GEORGE BERNARD SHAW PASSES ON



THE death occurred on the 2nd November, at 4-59 a.m. at his residence, in the little village of Ayot St. Lawrence, of this great man of arts, letters, philosophy, satire and controversy, at the ripe old age of 94.

In living to this age, G. B. S. divorced age from senility successfully. Our interest no. 1 lies in recording this fact. Longevity without senility is the objective of to-day's medicine. Up to the moment he stumbled, fell and broke his thigh a few weeks ago, he was actively engaged in his usual literary pursuits. In fact he had embarked on a new venture and was writing a guide book to the little village of his choice *in verse*, with photographs taken by himself.

This great teacher and artist, in his long life, accumulated, behind a translucent smoke screen of abruptness and levity, enormous stockpiles of knowledge of human nature and of wisdom. These he leaves to posterity.

The translucency of the screen was intriguing in the extreme and never really was absent even in apparently transparent situations, such as in a direct answer to a direct question:

Q. What is your honest opinion of G. B. S.?
Ans.G. B. S. is humbug.

(SIXTEEN SELF SKETCHES by Bernard Shaw, London. Constable and Company Limited, 1949, p. 54).

In the preface to the DOCTOR'S DILEMMA, which is nearly as long as the play itself, occur the following comments:

1. Medical Poverty

'To make matters worse, doctors are hideously poor. The Irish gentleman doctor of my boyhood, who took nothing less than a guinea, though he might pay you four visits for it, seems to have no equivalent nowadays in English society. Better he a railway porter than an ordinary English general practitioner.'

2. The Successful Doctor

'The doctor whose success blinds public opinion to medical poverty is almost as completely demoralized. His promotion means that his practice becomes more and more confined to the idle rich.'

3. The Psychology of Self-Respect in Surgeons

'The surgeon, though often more unscrupulous than the general practitioner, retains his self-respect more easily.'

4. Bacteriology as a Superstition

'The smattering of science that all—even doctors—pick up from the ordinary newspapers nowadays only makes the doctor more dangerous than he used to be They conceive microbes as immortal until slain by a germicide administered by a duly qualified medical man.'

Our interest no. 2 lies in representing to the profession these provocative subtleties. Their transparency is only apparent like the appraisal of his own worth by the sage.

His observations on non-violence also lie behind the screen.

'One of the first points of honour in civilized society should be that mental combats must not be fought out with fists nor crime by torture. Paul Jones's instinct was sound when he was prepared to kill a mutineer, but not to flog him' (SIXTEEN SELF SKETCHES, p. 104).

One of the major prophets of the age has passed over. He was a vegetarian, teetotaler and non-smoker.

He has gone in the splendour of his sunset (J. C. Trewin, *John O'London's Weekly*, 10th November, 1950, p. 585).

He was born in Dublin on 26th July, 1856, the third child and only son of George Carr Shaw, a civil servant with traditions of gentility unsupported by means. His early life at home was not particularly happy and his early education not very satisfactory.

He worked for several years in the office of a land agent.

'.....I found no difficulty in doing the work, and succeeded in changing my sloped, straggly, boyish handwriting for a very fair imitation of the compact script of my predecessor' (SIXTEEN SELF SKETCHES, p. 31).

At 20 he came to London where his mother, living separately from his father, was a singing teacher working in association with a gifted musician G. J. V. Lee, an eminent Dublin orchestra conductor. The association had started in Dublin many years previously.

In London he began life as an indifferent novelist, but succeeded later as an art critic.

'.....for the ignorance of daily newspaper editors of the fine arts at that time is now hardly credible, as their nightly-duties made it impossible for them to attend theatres or concerts. Any incomprehensible jargon could be palmed on them as art criticism.'

Only apparent transparency again. While humbug in art is readily admissible and found every day and everywhere in strong concentration, the sage as an artist and as an appraiser of art was always ahead of his contemporaries.

Then come ventures into socialism and studies into human nature which fructified into a 'spell-binding' oratory, over 50 plays and many books.

Marriage does not appear to have made much difference in the views of G. B. S.

'What can childless people with independent incomes, marrying at forty as I did, tell you about marriage?'

One wonders whether one has found a really transparent spot in the screen in this instance.

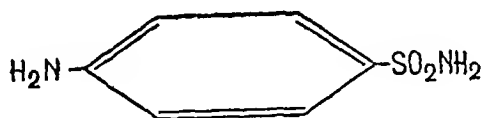
A reference to the last visit by the sage to his one surviving sister is equally dissociated from emotion :

'One afternoon, when her health was giving some special anxiety, I called at her house and found her in bed. When I had sat with her a little while, she said, "I am dying". I took her hand to encourage her and said, rather conventionally, "Oh no: you will be all right presently". We were silent then; and there was no sound except from somebody playing the piano in the nearest house (it was a fine evening and all the windows were open) until there was a very faint flutter in her throat. She was still holding my hand. Then her thumb straightened. She was dead.'

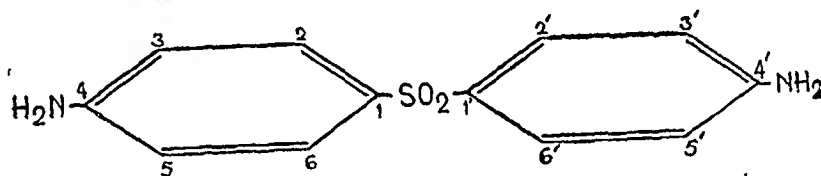
Views of G. B. S. on spiritual belief are rather far away from the screen, towards the centre of the stockpiles. The benefit of the last prayers of the Church of England, however, was given to him on his death bed (P. T. I. Reuter, *The Statesman*, Calcutta, 2nd November, 1950, Late City Edition).

SULPHONAMIDES AND SULPHONES

CERTAIN amount of confusion often arises between the two classes of drugs, the Sulphonamides and the Sulphones. The question often arises amongst the medical men, "what are the points of similarity and dissimilarity between these two classes of chemotherapeutic agents'. A sulphonamide is the amide of the corresponding sulphonic acid. It may be represented by the general formula $R.SO_2NH_2$, where R is any organic radical like CH_3 (methyl), C_2H_5 (ethyl), C_6H_5 (phenyl), etc. The simplest of the chemotherapeutically active sulphonamide and the parent substance of this group of drugs is *para*-aminobenzenesulphonamide or sulphamylamide (I). The more popular sulphonamides



(I)



(II)

such as sulphapyridine, sulphathiazole, sulphadiazine and sulphaguanidine are produced by replacing one of the H atoms attached to N of SO_2NH_2 by 2-pyridyl, 2-thiazolyl, 2-pyrimidyl and guanidyl radicals respectively.

The sulphones have the general formula $R.SO_2R'$, where R and R' are either similar or different organic radicals. The parent drug of the sulphone group is 4, 4'-diaminodiphenylsulphone (II). The common drugs of the sulphone group, e.g. Promin, Diasone or Diamidin, Sulphetrone or Novotrone, etc., are mostly derivatives of (II) with water soluble side-chains attached to the two N atoms. It is interesting to mention in this connection that the well-known hypnotic drug Sulphonal, $(CH_3)_2C(SO_2C_2H_5)_2$, is also a member of the sulphone group from the chemical standpoint.

R. C.

THE TREPONEMATOSES

THE relationship of the spirochaetes responsible for yaws and syphilis has for long been the subject of controversy, as has been the relationship between the two diseases themselves. It is well known that other disease syndromes with certain differing features, but related clinically either to yaws or syphilis, occur throughout the world. Examples are *bejel* of the Euphrates

Valley, the endemic *syphilis* of Bosnia, and *pinta* of the South Americas. These, and other clinical entities, have recently been the subject of increasing attention. Hudson's (1945) thesis of the relationship of yaws to syphilis, outlined in his monograph, is a masterpiece of observation and correlation between historical, geographical, racial and allied factors. Nevertheless, there exist much speculation and much controversial matter, and the clinical experiments of Akrawi (1949) point to the necessity of further work.

With the advent of the spirochætal immobilizing technique, discovered at the Johns Hopkins University by Nelson and Mayer (1949), there appears for the first time an opportunity to test the relationship of the various strains of spirochætes in the laboratory. The mechanism of immobilization is still to be worked out in detail, but there is little doubt that it is caused by an antibody distinct from the *reagin* tested for in the various serological tests for syphilis. Cross reactions with various strains of spirochætes are to be expected owing to similarity of chemical composition. Yet preliminary tests would indicate that the spirochætes of yaws and syphilis are two separate entities. Confirmatory tests are necessary. Similar tests would finally elucidate the relationships of other clinical entities, *bejel*, *pinta* and *endemic syphilis*.

Such tests would confirm what has been, up to date, impression and speculation. Clinical differences between yaws and syphilis are recognized. While syphilis is known to be a disease of urban areas, yaws has been usually noted in rural populations in the tropics. With major movements of large masses of population in areas of South-East Asia as a result of war conditions, and the growing movements of rural populations from the country to the cities as industrialization increases, the questions arise: shall we see an increase of yaws in cities, and *vice versa*, has syphilis increased in rural areas? Has the distribution between town and country been merely fortuitous, the result of different modes of living conditions in rural and urban areas, or has the presence of one disease brought about an 'immunization' of the population against the entry of the other?

These, and numerous other questions, are nearer to being solved to-day than ever before. The World Health Organization, in relation with the United Nations International Children's Emergency Fund, is launching a mass attack on the Treponematoses, a word now in common use for the whole gamut of such diseases. Teams of experts are already in Haiti, and preliminary investigations have been completed in Iraq, Yugoslavia, Thailand, Indonesia and the Philippines. Teams are due shortly to proceed to Thailand and to Indonesia. The combined experiences of these teams in the various countries, when completed, will make another contribution to help solve some of the numerous riddles of medicine. That global efforts towards

the solution of such problems can be undertaken by international bodies indicates another trend in medical thinking to-day.

N. K. J.

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Medical News

[The following 3 items are abstracted from W.H.O. Press Releases issued from Kandy, Ceylon.]

(1) THIRD SESSION OF W.H.O. REGIONAL COMMITTEE FOR SOUTH-EAST ASIA

INTERNATIONAL HEALTH PROGRAMMES IN THE REGION FOR 1951

(No. SEA/PR/49-50, dated 24th September, 1950)

INTERNATIONAL health programmes in S.-E. Asian countries for 1951, involving a total expenditure of over 4½ million dollars, were discussed at the morning's meeting of the Programme Sub-Committee of the Third Session of the W.H.O. Regional Committee for S.-E. Asia at present being held in Kandy, Ceylon.

The programmes proposed include assistance to countries of the region in strengthening their health administrations, statistical services and training facilities for medical and related personnel; projects for the control of malaria, tuberculosis, venereal disease, typhus, leprosy and yaws; research on problems of transmission of cholera and plague; the promotion of maternal and child health, environmental sanitation, BCG campaigns, and nutrition surveys; and the provision of fellowships.

This morning's discussion included projects for which W.H.O. gives technical approval and supervision and for which the U.N. International Children's Emergency Fund (UNICEF) furnishes supplies and equipment and in some cases bears the cost of international personnel. The UNICEF allocations in 1951 for such jointly-sponsored projects total \$3,400,000. The balance is provided from W.H.O.'s regular budget (\$584,000) and Technical Assistance Funds made available to W.H.O. by the United Nations (\$680,000).

Full details of the 1951 programmes in each country will be issued in the form of a report of the Programme Sub-Committee to the final plenary session of the Regional Committee.

Yesterday afternoon, after clearing up a number of minor points on its agenda, the Programme Sub-Committee discussed the problems of promotion of maternal and child health, school health and industrial health, and began consideration of possibilities of preparing essential medical supplies within the region.

It is increasingly realized, the sub-committee agreed, that mothers and children form a very important part of the population from the health point of view. It was essential to cultivate the study of child health under conditions existing in the region, where at the moment the care of children was left very much to chance. Deaths in S.-E. Asian countries in the age

Professor C. M. Hasselmann of Erlangen University, American Zone of Germany, as expert adviser for a yaws control project being conducted in Indonesia by W.H.O., the United Nations International Children's Emergency Fund, and the Indonesian Government.

Professor Hasselmann, the first German employed by W.H.O., has been Chairman of Dermatology and Venereology and Chief of Clinics at Erlangen University. The author of more than 100 scientific papers, Professor Hasselmann has spent some 20 years in the Far East, many of them in Manila as Sectional Chief at the American St. Luke's Hospital. Throughout World War II he lived in China where he taught public health and hygiene at the Pennsylvania Medical School, St. John's University, Shanghai.

Professor Hasselmann will leave Geneva this week for Indonesia, where he will succeed Professor Frederick R. Hill as expert adviser for the W.H.O.-UNICEF campaign against yaws, a tropical disease that affects the skin and often leads to incapacitation and lifelong disfigurement.

CULTIVATING GERMS—TO PRODUCE SULPHUR

(Reproduced from *Science and You*, UNESCO Features, No. 31, 15th October, 1950, p. 14)

By MAURICE GOLDSMITH
UNESCO Science Editor

DESERT lakes may soon provide the basis for a flourishing chemical industry. Two scientists from Britain's Chemical Research Laboratory, in the Department of Scientific and Industrial Research, have just completed an examination of lakes in Tripolitania and Cyrenaica, to explore the possibility for mass production of sulphur.

Sulphur is the best material for the manufacture of sulphuric acid. So essential to all industrial effort is this acid that the magnitude of a country's industrial activity can often be quite accurately calculated from its consumption of sulphuric acid at any time. It has been described as 'the barometer of business and civilization'. In the United States alone, 35,000 tons a day are used. With increasing industrial activity throughout the world the demand for sulphur is rising sharply, and its supply is of the greatest urgency for countries like Great Britain which have no native resources.

Sulphur seems to be produced in these lakes by certain biological processes, and the two British scientists had the task of finding out what really happens. The desert lakes are full of micro-organisms, known as sulphate-reducing bacteria, which reduce sulphates to sulphides. The sulphur can be produced from one of these, hydrogen-sulphide, by a simple process of aeration. However, the rate of production of sulphide by this method is low and to make the process worth while economically, it is necessary to speed up the process of reduction of sulphates about ten-fold. The research now being undertaken is concerned with this aspect.

Three main methods of research are to be employed. Strains of bacteria from various parts of the world will be examined for their speed of reduction, the influence of different environments will be investigated, and methods of obtaining possible quick reducing strains by artificial means will be explored.

Mr. K. P. Butlin and Mr. J. Postgate who made the examination reported that four lakes were examined and samples taken for later work. The first lake they found was a vivid milky blue with a broad band of red around its border. Arab workers plunged into the

lake and scooped up handfuls of yellow mud from the bottom. It was sulphur. There was a strong smell of hydrogen sulphide, which is an indication of the action of sulphate-reducing bacteria. The bottom of the lake was covered with a deposit of about 6 inches thick of finely divided sulphur. This formation of sulphur has since been reproduced artificially in the laboratory by incubating artificial lake water, based on an analysis of the original, with the red and green material and crude cultures of sulphate-reducers. Much sulphur was formed.

In the dry season, the Arabs scoop up the sulphur from the bottom of the lakes and leave it to dry. It is later collected into heaps for export or local use. The annual sulphur production of the lakes under natural conditions is approximately 200 tons.

Research is now aimed at the possibility of developing an industrial process based on what takes place in the lakes. One lake contains about half a million gallons and produces about 100 tons of sulphur a year. It has been suggested that natural waters could be exploited similarly; and sewage is an excellent medium for sulphate-reducers. It may even be found desirable to contaminate lakes in desert areas to facilitate this large-scale production of sulphur.

There was one immediate practical result from this expedition. Into Libya was being imported from Italy sulphur for use in dressing vines at a cost of £80 per ton. The annual tonnage needed is about 50 and as the lakes themselves produce about 200 tons a year, there is more than enough to supply these requirements. The scientists had seen dumps of crude sulphur near the lakes which can be delivered at Benghazi at £20 per ton. Of course, experiments will be necessary before this crude sulphur can be used on a large scale. But it is not believed that it is unsuitable, and its use would save the country several thousands of pounds per year.

Sulphuric acid is used in every aspect of our work-a-day world: in fertilizers, petroleum, chemicals, coal products, the iron and steel industry, rayon and cellulose film, textiles and explosives. It is certain that without this acid there would be the prospect of our facing a lower standard of technical civilization. Sulphur, which, in the early days of man, was believed responsible for the fiery lakes of hell, is to-day indispensable to us.

NEW APPOINTMENT FOR BLIND PHYSICIAN

DR. BEER RETURNING TO INDIA

(Reproduced from Release No. B.F. 1147, issued by British Information Services, New Delhi)

RETURNING to India with his wife to become head of the Physio-therapy Department of the Salvation Army's Emery Hospital at Anand, in Bombay State, is Dr. Stanley Beer, a blind British doctor who has spent 25 years in Gujarat.

Dr. Beer spent nearly four years with the Royal Army Medical Corps at Trimulgherry, near Hyderabad (Dn.) during World War I. After the war he returned to Britain to train as a Salvation Army Officer. At the end of his training he was sent to the Emery Hospital at Anand where he served first as nurse and dispenser before working for his medical degree and qualifying as physician and surgeon.

For 25 years Dr. Beer and his wife worked in Gujarat. Four years ago Dr. Beer's sight began to fail and he returned to the U.K. for treatment. An operation for cataract was unsuccessful and he became incurably and almost totally blind. Despite this great handicap he was determined to return to India in a useful capacity and has been studying physio-therapy

for the last three years under the auspices of the National Institute for the Blind. Together with the Salvation Army, the Institute has provided him with the very latest type of physio-therapy equipment for use at the Emery Hospital.

Dr. Beer, who is nearly 55 years old, is an expert braille typist and not only deals with all his own correspondence but with that of the family too. All four of his children were born in India, of whom two—one son and daughter—are now trained nurses.

DRUGS RULES, 1915

NOTIFICATION

1. (No. P.1-S/50-DC, Government of India, Ministry of Health, dated New Delhi, the 3rd October, 1950)

In exercise of the powers conferred by sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), the Central Government is pleased to direct that the following further amendment shall be made in the Drugs Rules, 1915, the same having been previously published as required by the said sections namely :—

In the said Rules, for sub-rule (2) of rule 1, the following sub-rule shall be substituted, namely :—

'(2) Parts I to IV extend to all Part A and Part C States. The remaining parts extend to Part C States only.'

(Sd.) J. N. SAKSENA,

Under Secretary.

2. (No. F.1-15/49-D, dated 26th October, 1950, Government of India, Ministry of Health, New Delhi)

The following Draft of certain further amendments to the Drugs Rules, 1915, which it is proposed to make in exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1950), is published as required by the said sections for the information of all persons likely to be affected thereby and notice is hereby given that the Draft will be taken into consideration on or after the 31st January, 1951.

2. Any objections or suggestions which may be received from any person with respect to the said Draft before the date specified will be considered by the Central Government.

Draft Amendments

In Schedule A to the said Rules—

1. In Form 20, to the conditions of licence the following shall be added, namely :—

'4. No sale of any drug shall be made for purposes of re-sale.

Provided that this condition shall not apply to the sale of any drug to—

(a) an officer or authority purchasing on behalf of the State Government, or

(b) a hospital, dispensary, medical or research institution or registered medical practitioner for supply to his own patients.'

2. In Form 21, to the conditions of licence the following shall be added, namely :—

'4. No sale of any drug shall be made for purposes of re-sale.

Provided that this condition shall not apply to the sale of any drug to—

(a) an officer or authority purchasing on behalf of the State Government, or

(b) a hospital, dispensary, medical or research institution or registered medical practitioner for supply to his own patients.'

(Sd.) J. N. SAKSENA,

Under Secretary.

3. (No. F.7-11/48-DS, dated 27th October, 1950, Government of India, Ministry of Health, New Delhi)

The following Draft of a further amendment to the Drugs Rules, 1915, which it is proposed to make in exercise of the powers conferred by clause (f) of sub-section (2) of Section 12 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said section for the information of all persons likely to be affected thereby and notice is hereby given that the Draft will be taken into consideration on or after the 1st February, 1951. Any objections or suggestions which may be received from any person in respect of the said Draft before the date specified will be considered by the Central Government.

DRAFT AMENDMENT

'In the Drugs Rules, 1915, after Rule 43, the following rule shall be inserted, namely :—

'43A. No drugs shall be imported into India except through one of the following places, namely :—

Ferozepore Cantt. and Amritsar Railway Stations

In respect of drugs imported by rail across the frontier with West Pakistan.

Ranaghat, Bongaon and Mahiassan Railway Stations

In respect of drugs imported by rail across the frontier with East Pakistan.

Castle Rock Railway Station

In respect of drugs imported by rail across the frontier with Goa.

Madras, Calcutta and Bombay

In respect of drugs imported by sea into India.

Madras, Calcutta, Bombay, Delhi and Ahmedabad

In respect of drugs imported by air into India.'

(Sd.) J. N. SAKSENA,

Under Secretary.

DRUGS ACT, 1940

Copy of Notification No. F.1-11/50-DS, dated the 17th October, 1950, from the Ministry of Health, addressed to the Publisher, *Gazette of India*, New Delhi.

In pursuance of sub-section (2) of Section 16 of the Drugs Act, 1940 (XXIII of 1940), the Central Government hereby gives notice of its intention to make the

following amendment in the Schedule to the said Act, with effect from the 1st February, 1951.

DRAFT AMENDMENT

In the entry under the heading 'Standard to be complied with' against item 4, 'Other Drugs' in the Schedule to the said Act, for the words 'latest edition of the British Pharmacopœia' the words 'current edition for the time being of the British Pharmacopœia' shall be substituted.

STUDIES IN ANTIMALARIALS

BIGUANIDO-ARYL-SULPHIDES AND SULPHONES

(Abstracted from a communication by A. C. Roy, M. Raghavan and P. C. Guha of the Organic Chemical Laboratories, Indian Institute of Science, Bangalore, to the Editor, *Current Science*, Vol. 19, No. 6, June 1950, pp. 177)

FOLLOWING the discovery of the unique antimalarial properties of paludrine, many attempts have been made to improve upon the activity of the parent drug. Considering that a suitable substituted biguanide system may be sufficient for antimalarial activity, we have prepared a series of N¹-N²-aryl substituted biguanides as possible antimalarials, by replacing the isopropyl group in paludrine and its bromoanalogue with chemotherapeutically active residues of 4-nitro-4'-amino diphenyl sulphide, 4, 4'-diamino diphenyl sulphone, 4, 4'-diamino diphenyl sulphone.

The chemotherapeutic activities (antimalarial and antitubercular properties) of the compounds are being tested.

Full details will be published elsewhere.

KOCH AND CHOLERA

(Reproduced from the *Practitioner*, Vol. 164, No. 984, June 1950, pp. 478)

AN interesting sidelight on the discovery by Koch of the vibrio as the causative organism of cholera is revealed in Sir Leonard Roger's reminiscences 'Happy Toil' (which is reviewed in the *Indian Med. Gaz.*, Sept. 1950, p. 430). A distinguished I.M.S. officer, N. C. Macnamara, subsequently a Vice-President of the Royal College of Surgeons of England, as a result of his work on cholera in India became convinced of the infective nature of the stools in this disease. He therefore spent part of his leave in 1882 studying the then new subject of bacteriology with Koch in Berlin. 'Thereafter', according to Sir Leonard, 'in February 1883 he offered his services to the India Office, as he wished to go to Egypt, where cholera was then prevalent, to work at its bacteriology. His application was refused by the Secretary of State for India; yet eight months later Koch was given every facility for his investigations in Egypt which resulted in the discovery of the cholera vibrio'. There will be few who will disagree with Macnamara in his comments on this episode that it enables one 'to understand why an Englishman, and one of the Indian Medical Service, had not the privilege of discovering the cholera

bacillus'. It is certainly no depreciation of the pioneer work of Koch to suggest that in this particular instance he owed the privilege of discovering the cholera vibrio to the obtuseness of Whitehall.

FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

(14TH OCTOBER, 1950)

THE following students were declared to have passed the L.T.M. examination, session 1950.

Passed

- Dr. Kamalaksha Das, L.M.F. (Bengal), Private Practitioner.
- Dr. Surath Lal Das, L.M.F. (Bengal), Private Practitioner.
- Dr. Kali Kinkar Dutt, L.M.F. (Bengal), Private Practitioner.
- Dr. Kali Pada Ganguli, Certificate of West Bengal State Medical Faculty under Article 6C, Medical Officer, Union Drug Co., Ltd., Calcutta.
- Dr. Shib Narayan Ghatak, L.M.F. (Bengal), Assistant Medical Officer, Fort Gloster Jute Mills, Howrah.
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- Dr. Dattatraya Vishnu Indollikar, L.M.F. (M. P.), Assistant Surgeon Gr. II, B. N. Rly. Workshop, Nagpur.
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- Dr. Ganesh Chandra Pushilal, L.M.F. (Bengal), Private Practitioner.
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Public Health Section

MUSHROOM POISONING IN INDIA

By S. D. S. GREVAL

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Toxicologists in India do not appear to have been struck so far by mushroom poisoning. For many years the solitary case described was that of a Collector who, half a century ago, laughed in an indignant manner in his Court after consuming mushrooms at breakfast (Chevers, quoted by Modi, 1949). Dried mushrooms from Kashmir are consumed as delicacies in the Punjab as *khumb*, *guchchi* or *dhingri* without any untoward effect on physiology or dignity. In the East Punjab the rural population collects and consumes mushrooms during the rainy season. The village folk make a distinction between *khumb* (mushroom) and *bahera* (toad stool) only; the former is firm and grows for several days while the latter is soft and lasts only a day. The *khumb* is white in colour but may be in shape open like an umbrella or close like an egg attached to a stalk. The *bahera* is always open and may be white, fawn or grey in colour. No attention is paid to the 'gills' for differentiation. Very recently untoward effects have been reported (see below).

She had taken some rice and cooked mushroom in the morning and developed the condition about half an hour after taking the food. Within 10 minutes of arrival at hospital she began to develop the symptoms of acute mushroom poisoning with profound excitement, intoxication, delirium with stupor and occasional convulsions. The pupils were contracted, and there was frothing at the mouth and nostrils.

'Emetics were given at once, and in time the woman vomited all the stomach contents consisting of food and particles of cooked mushrooms. An injection of atropine was given as an antidote, and with some stimulants and warmth the patient had an uneventful recovery within 8 hours' (Gupta and Halder, 1943).

(2) *Severe cases*.—For the following account the writer is indebted to the authorities of the Government Headquarters Hospital, Ootacamund (R.O.C. No. 2196/50, dated 14th October, 1950):—

'On 17th July, 1950, two families, both estate labourers working in a tea estate, ten miles away from Ootacamund, ate cooked mushrooms for their evening meal. The mushrooms were picked up by the children from an adjoining small forest of their lines when the adults were away working. The children cooked the mushrooms into a curry adding chillies, salt and curry powder. The cooking was done in the Indian way.

'Early next morning, i.e. eight to ten hours after the meal, they developed signs and symptoms of acute gastro-enteritis. Nine persons were admitted into the hospital by 3-30 p.m. on 18th July, 1950. The rest, i.e. three, were admitted on 19th July, 1950, most probably their symptoms may have been mild or they developed them later on.

Serial number	Age	Sex	Admission	Discharged cured	Died
1	40	Male	18-7-50, 3-30 p.m.	25-7-50	..
2	35	Female	Do.	23-7-50	..
3	9	Male	Do.	25-7-50	..
4	8	Do.	Do.	..	19-7-50, 4 p.m.
5	7	Do.	Do.	..	20-7-50, 3 a.m.
6	7	Do.	Do.	..	21-7-50, 12-30 a.m.
7	6	Do.	Do.	..	19-7-50, 2-45 p.m.
8	6	Female	Do.	..	19-7-50, 8-30 a.m.
9	4	Do.	Do.	..	19-7-50, 7-45 a.m.
10	40	Male	19-7-50, 4 p.m.	21-7-50	..
11	30	Female	19-7-50, 12 noon	..	20-7-50, 12-35 p.m.
12	15	Do.	Do.	23-7-50	..

It could be considered reasonable to ascribe the harmlessness of the fungus to the Indian cooking which involves a preliminary frying in cooking fat (usually *ghee* in the Punjab) and a subsequent simmering at low heat for an hour or longer. That there are certain volatile and thermo-labile substances in the fungus is known. They are likely to be eliminated in the processes of drying, frying and simmering.

Poisonous mushrooms, however, are met with in India (Owens, 1935).

Recent cases: (1) *A mild case*.—On 12th April, 1943, a female garden labourer, aged about 38 years, came to the hospital in a condition of extreme intoxication, being supported by her husband.

'At the time of admission the patients looked very ill, sunken eyes, rapid feeble pulse, no cramps, nobody was unconscious. The vomiting had stopped, but the diarrhoea continued. Their diarrhoea stopped, they looked apparently well. But later they complained of severe abdominal pain which lasted for one to two hours before they were dead. They remained conscious to the end.

'The motion and rectal swabs were sent for culture and were negative for cholera vibrio.'

Serious cases have also been reported from Assam (Scal, personal communication, 1950).

In three villages, two near Dibrugarh and one a tea estate, 15 persons were affected and 10 died.

The following account has been obtained from a member of a family affected in the Punjab in August 1948:—

My village, Katani Kalan, is about 14 miles from Ludhiana and situated in the angle between a road and a canal. In the south of the village is our land watered from a well. In one plot we had grown sugarcane. In this plot I found mushrooms of which I gathered about a seer and took them home. I curried them after a preliminary frying in ghee. The frying lasted about two minutes and simmering later about half an hour.

My mother prepared *chapattis* and all of us, five in number, ate the food.

After about 2 hours we were all vomiting. We recovered in about 8 hours.

Identification, etc., of the mushroom.—No work appears to have been done in India on the classification of mushrooms. The usual brief accounts given in the English and American books are accepted and followed. According to these accounts: (1) The usual edible mushroom in England is the meadow or field mushroom, *Agaricus campestris*. It has a small food value, more than 50 per cent of the nutritive matter being protein. The percentage is higher in the young than in the old mushrooms, and in the head than in the stem. The water content is about 80 per cent. The fat content is negligible. Some minerals and a carbohydrate trehalose, yielding largely mannite on drying, are present (Parkinson, 1947). (2) The poisonous mushrooms are mostly *Amaneta phalloides*, *A. muscaria* and *A. verna*. Muscarine and several other toxic substances are responsible for the effects. (For a similar account see Chopra, 1936.)

The only comprehensive study of tropical mushrooms appears to have been undertaken in the Philippines (Mendoza, 1938).

Three types of poisoning occur: (i) Gastro-intestinal type. Vomiting, colic, thirst and collapse are the dominating symptoms. The prognosis is fair. (ii) Nervous type. Headache, somnolence, trismus and midriasis occur. Muscular cramps and opisthotonos may be added and so may be blindness, loud cries and finally coma. The prognosis is not so good as in the other type (Alvarez, 1947). (iii) Allergic type. Some people are allergic to mushrooms of any kind (Parkinson, *loc. cit.*).

Treatment.—The rabbit seems to carry the neutralizing substances, chopped up stomach for the gastro-intestinal toxin and brain for the neurotoxin. The fresh, chopped-up organs from several animals, by mouth are specific. The usual supportive treatment and atropine as an antidote to muscarine are indicated. For allergic manifestation, adrenalin, etc., must be employed.

A serious difficulty in applying the specific treatment arises: In India rabbits are available in large towns only, while cases of mushroom poisoning are likely to occur in villages and small towns.

Precautions against mushroom poisoning.—The fungus or the method of cooking it should have

the approval of the *local* inhabitants. There are no simple distinctions between the poisonous and non-poisonous mushrooms. This warning is specially applicable to displaced persons finding new homes.

A speculation presents itself: Dearth of cooking fat and oil may be responsible for insufficient frying (a preliminary process in currying). Dearth of fuel may be responsible for insufficient simmering. These dearths are becoming universal in India. Hence the need for warning.

Medicolegal points.—In addition to cholera and food poisoning by the food poisoning organisms (including those in duck egg), poisoning by arsenic and antimony, etc., should also be excluded. In the present troubled times all is possible, specially where displaced persons are concerned.

Supplement to food grains.—Nutritionally edible mushrooms, in spite of the risk which can be eliminated, deserve a consideration. They have a small food value and when dried are transportable like food grain. They may be cultivated as they are on the continent of Europe.

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EFFICACY OF PENICILLIN IN REDUCING BACTERIAL CONTAMINATION IN VACCINE LYMPH

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THE great difficulty, which almost every lymph establishment in this tropical country encounters, is in regard to the total bacterial

count in lymph. Hence every establishment undertakes some sort of treatment of lymph prior to issue with chloroform, clove oil, phenol or the latest, penicillin. The information on the efficacy of penicillin on lymph samples has been given from the Belgaum Vaccine Institute by Patel (1948).

The object of the present paper is to corroborate the previous findings and also to point out the difficulties that have been met. From the small number of experiments made by the writer it seems that the following factors come into play in assessing the results from penicillin treatment :—

1. Concentration of lymph (in 50 per cent glycerine distilled water solution).
2. Bacterial flora present in the samples.
3. Type of penicillin used—preponderance of 'G' or 'K' factor (in coloured penicillin) in the penicillin.
4. Dose of penicillin.
5. Period of contact with penicillin.
6. Effect on streptococcus and anaerobes.
7. Bacteriostatic effect—duration.
8. Effect on potency.

1. Concentration of lymph

Lymph samples in 1 in 5 dilution have been tested with the different concentrations of penicillin. No additional treatment was done.

2. Bacterial flora

As is well known, different lymph samples vary with regard to the bacterial flora—some samples showing preponderance of gram-positive and gram-negative bacilli, gram-negative diplococci, as well as in a few instances, gram-positive diplococci on which penicillin has been found to be of little effect, after a varying period of contact. Hence prior to treatment with penicillin an examination has been made for the bacterial flora. Some samples containing positive anaerobes and streptococcus have also been specially selected for the experiments.

It will be seen from table I that the total bacterial counts in different samples vary to a great extent (after contact with penicillin) and the bacterial flora in some samples has been acted on promptly and vigorously while in others only sluggishly. This is evidently due to different flora present in samples.

3 and 4. Type of penicillin used and its dose

Two types of penicillin have been used : (i) Crystalline penicillin sodium 'G'. (ii) Coloured penicillin containing high 'K' factor.

[Obtained from Messrs. Imperial Chemical Industries (India) Ltd.].

Table I shows that coloured penicillin containing high 'K' factor is much more powerful

in vitro in reducing the bacterial count than penicillin 'G'. Bacterial reduction is more pronounced within a much shorter period with the coloured penicillin than with the penicillin sodium 'G'.

Dose of penicillin

It seems to be interrelated with the period of contact. If the period of contact is longer than one week, as table I (samples 1 to 3B), smaller dose of penicillin will suffice but in that case one derives no extra advantage, as there are other much cheaper methods of purifying lymph (by chloroform or clove oil).

The aim has been to find out if this period of contact can be reduced to the minimum and to increase correspondingly the dose of penicillin for this purpose to make it effective without lowering the potency of lymph (see tables I and II for observations in a few samples of the series).

Samples 1 to 3B	..	{	Penicillin used	150
			units per cc.	
Samples 10 to 12A	..	{	Penicillin used	300
			units per cc.	

TABLE I

Effect of penicillin 150 units per cc. on total bacterial count (no other treatment)

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Type of penicillin used	Duration of contact	Result after 48 hours' incubation
1	'G' 150 units	10 days	400 per cc.
{ 1B	'G' 150 "	10 "	1,500 " "
{ 1B1	'K' 150 "	3 "	2,000 " "
{ 2	'G' 150 "	10 "	7,000 " "
{ 2A	'K' 150 "	3 "	4,300 " "
{ 3A	'G' 150 "	9 "	5,700 " "
{ 3B	'K' 150 "	3 "	4,100 " "

TABLE II

Effect of penicillin 300 units per cc. on total bacterial count (no other treatment)

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Type of penicillin used	Duration of contact	Result after 48 hours' incubation
{ 10	'G' 300 units	2 days	2,800 per cc.
{ 10A	'K' 300 "	2 "	700 " "
{ 11	'G' 300 "	2 "	Sterile. " "
{ 11A	'K' 300 "	2 "	" " "
{ 12	'G' 300 "	2 "	600 per cc.
{ 12A	'K' 300 "	2 "	Sterile. " "

5. *Period of contact*

(i) Penicillin sodium 'G' 150 units per cc. of lymph (1 in 5) required about a week to bring down the count (table I, samples 1, 1B, 2, 3A and 3B).

(ii) With the same antibiotic with 300 units per cc. of lymph (table II, 10 to 12A) bacteriostatic effect was evident after 48 hours (10 to 12A)—count ranging within 3,000 per cc. Side by side, with coloured penicillin containing high 'K' factor: Within 48 hours the total count in some samples comes down to sterility and in other samples it remains within the count of hundreds per cc.—showing that the coloured penicillin is much more prompt in reducing the bacterial count. It has been noted that wherever the total count has been higher a preponderance of gram-negative and gram-positive bacilli (diphtheroids) and gram-negative diplococci and in few instances gram-positive diplococci and staphylococci has been detected. It may be stated from table II that the total count, whatever may be the variations after the varying periods of contact, has been always much below the standard laid down for it.

6. *Effect on the elimination of streptococcus and anaerobes*

As observed by Patel (1948), samples showing the presence of anaerobes clear up after a varying period of contact and hence this treatment is certainly an advance on the method of purification. Excepting sample 7 in table III, which showed persistent positive reaction in glucose broth (but negative in cooked meat), all other positive samples became negative even as early as between 5 to 10 days and remained persistently sterile even up to 4 months (*see* table III for observations in a few samples of the series).

TABLE III

Effect of penicillin on anaerobes in lymph

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Samples [-] are same samples.

Sample number	Result previous to treatment	Period of contact	Result after contact
1-'G'	C.M. } + G.B. } +	10 days After 4 months	Negative in both medias.
1B-'G'	C.M. } + G.B. } +	10 days After 4 months	Do.
1B1-'K'	C.M. } + G.B. } +	5 days After 1 month	Do.
9-'G'	C.M. } + G.B. } +	5 days After 1 month	Do.
9A-'K'	C.M. } + G.B. } +	5 days After 1 month	Do.
7-'G'	C.M. — G.B. +	10 days After 3 months	G.B. +.
7A-'K'	G.B. + G.B. +	10 days After 3 months	G.B. —.

G.B. = Glucose broth.

C.M. = Cooked meat.

Regarding streptococcus (whether haemolyticus or viridans) both appear to be affected by penicillin in dose of 150 units per cc. (*see* table IV for observations in a few samples of the series).

TABLE IV

Effect on streptococcus

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Penicillin 150 units per cc.

Sample showing positive streptococcus	Period of contact	Effect on streptococcus
{ 3A-'G' 3B-'K' 5-'G'	9-6-49—10 days 12-9-49—3 days 8-7-49—5 days	Negative. " "
{ 6-'G' 6A-'K'	8-7-49—8 days 8-7-49—8 days	" "
Penicillin 300 units per cc.		
{ 10-'G' 10A-'K'	30-8-49—2 days 30-8-49—2 days	" "
{ 11-'G' 11A-'K'	30-8-49—2 days 30-8-49—2 days	" "

7. *Bacteriostatic effect and its duration*

The bacteriostatic effect as already stated (table V) commences in about a week after treatment with penicillin 'G' 150 units per cc. With higher dose of 'G' 300 units, it is evident even after 48 hours. The effect of penicillin 'K' in the above strengths is much more pronounced. The loss of this bacteriostatic effect to some extent is seen after a month or so of treatment—the total count going up in some instances (7, 9A, 11, 11A, table V). But samples treated with coloured penicillin as

TABLE V

Variations in total count after penicillin treatment and storage

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Duration of storage	Variations
7 penicillin 'G'	2 months	Rise to 6,000 (from 1,400).
9A " 'K'	Do.	" " 1,500 (from 200).
11 " 'G'	1 month	" " 3,000 (from sterility).
11A " 'K'	5 days. Do.	" " innumerable.

well as some other samples in table VI did not show much variations after storage. It may be noted that, even after loss of bacteriostatic effect to some extent the total count does not go above the standard laid down in penicillin treated samples.

TABLE VI

No appreciable effect after storage in total count

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Units and type of penicillin used	Duration of storage	Variations
7A	'K'—150 units	2 months	Rise to 600 (from 500).
8	'K'—150 "	Do.	Rise to 900 (from 500).
9	'G'—300 "	1 month	Rise to 2,000 (from 2,300).
10	'G'—300 "	5 days.	Do.
10A	'K'—300 "	Do.	Rise to 4,000 (from 2,800).
			Rise to 1,200 (from 700).

8. Effect on potency

This matter has been elaborately studied in the article by Dr. Patel in October 1948 issue of the *Indian Medical Gazette*. Samples were kept below -10°C .

(1) Within 2 or 3 weeks after treatment with penicillin with the strength of 150 units or 300 units, the potency is not affected at all—reactions being confluent vesicles even in 1 in 10,000 dilution. But after 3 or 4 months with 150 units of penicillin ('G' or 'K') reactions in 1 in 2,000 dilutions have been either semi-confluent or discrete in samples 1 to 3B (table VII).

(2) With 300 units of penicillin (table VIII), 'G' or 'K': After 12 days' contact (samples 9 to 12A) the potency has not been affected but after 1½ months in most samples reactions have been semi-confluent or discrete in the same dilutions (table VIII).

Absence of full confluent reactions in all samples (though reactions within standard), in 1 in 2,000 dilutions after contact over 1½ months, may be noted. (For observations in a few samples of the series, see tables VII and VIII.)

But field tests with such samples have given about 99 per cent of case success with each

TABLE VII

Penicillin 150 units per cc.—1 in 2,000 dilutions of lymph

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Date of treatment	Date of 1st test 1 in 10,000 dilutions	Result of 1st test 1 in 10,000 dilutions	Date of 2nd test 1 in 2,000 dilutions	Result of test 1 in 2,000 dilutions
1-'G'	8-6-49	10-7-49	Confluent	8-10-49	Semi-confluent.
1B-'G'	8-6-49	8-10-49	Do.
1B1-'K'	12-9-49	8-10-49	Do.
2-'G'	8-6-49	10-7-49	Confluent	8-10-49	Discrete vesicles.
3A-'G'	8-6-49	10-7-49	Semi-confluent	8-10-49	Do.
3B-'K'	12-9-49	8-10-49	Do.

TABLE VIII

Penicillin 300 units per cc.—1 in 2,000 dilutions of lymph

'G' = Crystalline sodi 'G'.

'K' = Coloured penicillin.

Sample number	Date of treatment	Date of 1st test 1 in 2,000 dilutions	Result of 1st test 1 in 2,000 dilutions	Date of 2nd test 1 in 2,000 dilutions	Result of 2nd test 1 in 2,000 dilutions
9-'G'	28-8-49	9-9-49	Confluent	12-10-49	Semi-confluent.
9A-'K'	28-8-49	9-9-49	Do.	12-10-49	Do.
10-'G'	28-8-49	9-9-49	Do.	12-10-49	Discrete vesicles.
10A-'K'	28-8-49	9-9-49	Do.	12-10-49	Do.
11-'G'	28-8-49	9-9-49	Do.	12-10-49	Semi-confluent (†).
11A-'K'	28-8-49	9-9-49	Semi-confluent	12-10-49	Do.
12-'G'	28-8-49	9-9-49	Confluent	12-10-49	Semi-confluent (†).
12A-'K'	28-8-49	9-9-49	Do.	12-10-49	Discrete vesicles.

sample even after contact with penicillin for over 4 months. General reactions extremely mild and local reactions showing typical vaccinia.

Conclusions

(i) Penicillin appears to be a good bacteriostatic agent in concentration of 150 units or 300 units per cc.

(ii) Greater the concentration of penicillin (300 units per cc.) earlier is the purification.

(iii) Coloured penicillin (Messrs. Imperial Chemical Industries) is more powerful than penicillin sodium 'G'—not only *in vitro* but also in field tests.

(iv) Anaerobes and streptococcus are eliminated after a varying period of contact.

(v) Potency is not affected within 2 or 3 weeks but after long storage over 1 month or so may be affected to some small extent, though field tests have given quite good results.

(vi) Only the question of cost, particularly when a very large number of samples are to be issued daily, is a drawback to its general application.

(vii) As an emergency measure it is efficacious.

I am greatly indebted to my chief, the Health Officer, Calcutta Corporation, for guiding me in the work and permitting me to send it for publication.

REFERENCE

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The Indian Medical Gazette Fifty Years Ago

THE ANNUAL REPORTS OF THE LUNATIC ASYLUMS OF BENGAL, MADRAS AND THE PUNJAB FOR 1899

(From the *Indian Medical Gazette*, November 1900, Vol. **35**, p. 437)

THE blue, red and yellow covers of these reports are almost as varied as the conditions that obtain in the asylums of the three local Governments mentioned. That is what might be expected in a country so backward as India is in regard to both the legislation for, and treatment of, the insane. As time goes on, and as improvements are introduced by degrees, so gradually also will the conditions of the insane in the various presidencies and provinces of India be assimilated. To illustrate these differences, let us compare what is done to give instruction in mental diseases and training in the treatment

of the insane, also let us see what is provided in the way of occupation and amusement.

In the Punjab asylums apparently nothing was done to provide the patients with amusement. In the asylums of Bengal we read that the patients have musical instruments, a small library of vernacular books, cards, pet animals and birds; that *nautches*, sweetmeats and fruits are furnished on festival days, that the quieter patients are taken to visit the Zoological Gardens and the bazar, and that regular walking exercise is insisted on for those that decline work. This is all done on the initiative of the various superintendents; but in the Madras Presidency, we are glad to note that certain native noblemen, men of position and wealth, and others, take a kindly interest in their mentally afflicted fellow countrymen. Two rajahs sent frequent presents of fruit, other notables took a special interest in the asylum inmates, a Parsi opera troupe gave free admissions to selected insanes, and a native dramatic troupe gave a gratuitous performance in the asylum premises. In addition to this mention is made of games, juggling and aerobatic performances, monthly treats of music and light refreshments, a special Christmas treat with the distribution of small presents, chess and cards, domestic pets, and local sight seeing.

In the Madras asylums gardening and weaving are the chief employments; but we see with pleasure that advantage is taken of the inmates in aiding the asylum staff in all departments, just as is the case in well-conducted European asylums. Corn-grinding, coir yarn-twisting, mat-making, light tin-work, and needlework are also mentioned.

In Bengal asylums the inmates are largely employed in cultivation, dairy-farming, weaving, mustard oil manufacture, dry-earth preparation, needlework and domestic duties. Although no work is compulsory, yet the principle is recognized that the more the inmates can be induced to take up some employment, the quieter and more contented they become. Unfortunately this does not apply with equal force to the European and Eurasian insanes in Bengal, for whom the resources of work and amusement are considerably less than in Madras.

In the Punjab asylums the inmates were put to garden work in only one of the two asylums; manufactures of various kinds are alluded to, but the making of *munj* matting is the only one specified. In the Punjab practically nothing is done for the systematic teaching of mental diseases and their treatment. The same may be said of Bengal, though it is stated that arrangements are going to be made for the training of civil hospital assistants by attaching them on recruitment for a couple of months to asylums. But both in Bengal and the Punjab the teaching and training of asylum attendants is a haphazard business; 'warders' or 'keepers' they

are called, and virtually warders they will remain as long as they are recruited from the present class of men and women with their present pay and prospects, and so long as criminal and non-criminal insanes are herded together. The medical authorities are fully alive to the inferior quality of the asylum attendants, and the Director-General of the Indian Medical Service strikes the right note when he suggests the abolition of all forms of restraint, and he sees no reason why the Indian attendant should not be as much improved as the modern British one. A stumbling block exists in the association of criminal and non-criminal lunatics, because the former require a different kind of watch and ward for very obvious reasons.

In Madras the superintendent is also lecturer on mental diseases and gives clinical instruction at the asylum, and his assistant surgeon acts as assistant teacher, both of them drawing special allowances for their teaching work debitable to the Medical College. The list of the asylum staff in Madras compares very favourably with the somewhat meagre staff in the Bengal and Punjab asylums.

In the Punjab there have hitherto been two asylums, one at Lahore, and the other at Delhi. The former has accommodation for 296 persons, and 150 is the capacity of the latter. There has been a steady increase in the population of the Lahore Institution, so much so that there was distinct overcrowding, the total daily average strength having been 298.87 and a maximum of 319 at one time having been reached. The increase at Delhi has also been steady, and the maximum number confined at one time reached within one of the authorized scale, while the daily average total was 139.96. The question of accommodation in these asylums need no longer cause anxiety, because they have been abolished, and all patients have been transferred during the current year to the new Central Lunatic Asylum for the Punjab at Lahore. With this fresh departure, it is to be hoped, there will be a new régime for both *aliénistes* and *aliénés*.

In Bengal, too, there are signs of impending change. The six asylums are to be reduced to four by having a large central lunatic asylum at Berhampur, which will absorb the populations of the present Dullunda, Patna and Berhampur asylums, leaving Bhawanipur (for Europeans), Dacca and Cuttack asylums as before. The question of a central asylum has been on the tapis for the past five years, and one good result of the delay has been that the original scheme has been relegated to the limbo of the might-have-beens. The Inspector-General is to be congratulated on having induced Government to desist from the Bandel or Chinsurah project, which was at one time so much in favour. The population of the Bengal asylums is not on the increase, because we find the daily average

strength for 1899 was 902.84, which is less than in any of the previous ten years.

In the Madras Presidency there are three asylums, which are situated in Madras, Vizagapatam and Calicut. Of these the first is by far the most important. At present there appears to be no indication of new asylums in prospect, and there seems no need since the accommodation is ample. At the same time we note that numerous additions and improvements have been made, e.g. an isolation section of four blocks, covered passages, a noisy enclosure and dining-shed, etc.

In the Madras Institution the capacity is estimated at 689, whereas 446 was the maximum number on any one day; at Calicut there is accommodation for 133, and the maximum was 81; and at Vizagapatam there was a maximum of 76, while 91 can be received.

Current Topics, Etc.

Resistance to Proguanil

(From the *British Medical Journal*, i, 21st January, 1950, p. 171)

THE unpredictable adaptability of living creatures which excites the wonder and admiration of the philosopher is apt to give rise to other and less pious thoughts in the mind of the chemotherapist. Too often has his apparently ideal remedy been by-passed by the emergence of a resistant strain of the micro-organism to which it was at first lethal. The generally accepted explanation of this phenomenon is a simple one: among the many millions of organisms which are present in every infection there occurs an occasional variant which, either by the possession or by the lack of some special character, is so constituted as to be insusceptible to the action of the drug, while its less fortunate relatives are being killed off the variant multiples and in time replaces them, thus establishing a resistant race. For reasons which are not yet fully understood the faculty of provoking resistance is confined to certain types of drug. It is, for example, well known in relation to trypanamide, the sulphonamides and certain antibiotics. Fortunately it is not a characteristic of most antimalarial drugs, though the experience of Fairley and his colleagues with the Aitape-Wewak strain of *Plasmodium falciparum* suggests that resistance to mepacrine may occasionally develop. To this rule proguanil ('paludrine') is an exception. In the last few years proguanil-resistant strains of *P. gallinaceum*, *P. lophurae*, *P. cynomolgi*, and finally *P. vivax* and *P. falciparum* have been produced experimentally and, with one exception, have been transmitted by the insect vector without losing this property. This ominous series of laboratory findings has been followed all too soon by evidence which suggests that some similar process can take place in natural conditions. From Africa have come complaints of a 'break through' of malarial infection in individuals who claimed to have taken a suppressive dose of proguanil with unfailing regularity. Covell and his co-workers, in a series of carefully controlled experiments in patients infected with a West African strain of *P. falciparum*, found that proguanil alone failed to effect a radical cure. In India Chaudhuri

had a similar experience. These findings do not of course furnish any evidence of drug resistance, but they do indicate that different strains of parasites may have different degrees of susceptibility of proguanil.

In July 1949, Drs. J. W. Field and J. F. B. Edeson reported briefly from Malaya observations which have been extended and are given in more detail elsewhere in this issue. Since 1945 proguanil has been used for malaria suppression in certain rubber estates in Malaya. The few cases of overt malaria which occurred in this area were, until 1948, treated successfully with a single dose of proguanil. In 1949 a change became obvious, and one out of every four cases, treated with two or three times the dose previously given, failed to respond. Five cases of *P. falciparum* infection are recorded in which repeated therapeutic courses of proguanil did not effect cure. There seems little doubt that this disappointing experience is attributable to a proguanil-resistant strain of the parasite brought into being by the inefficient use of proguanil for suppression. Before accepting this conclusion as final, however, it would be advisable to bring the strain to Britain and have its properties tested under controlled experimental conditions.

The implication of these findings, if the explanation put forward proves to be correct, are far reaching and important. Edeson and Field admit that the present position is not serious, but fear, with good reason, that it may become progressively worse. Resistance is most likely to develop when relatively heavy blood infections are exposed to the action of sublethal doses of the drug, a state of affairs which may often arise during casual and irregular suppression, particularly in a hyperendemic area. Those with experience in enforcing preventive measures against malaria know how difficult it is to ensure that suppressive drugs are taken regularly, and in this case the shortcomings of the few can become a menace to the entire community. Thus, unless proguanil suppression can be carried out efficiently, it may be necessary to make use of some other compound which does not provoke resistance, such as mepacrine or chloroquine or, as Edeson and Field suggest, to alternate proguanil with these other drugs. The problem is a difficult one and calls for much careful consideration.

The following two items are reproduced from Surgical Newsletter, No. Wa 277, dated July 1950, prepared by the American Medical Association:—

Parenteral Nutrition in the Surgical Patient as provided from Glucose, Amino Acids and Alcohol

RICE and his associates discuss the nutritional requirements of surgical patients and say that they have used a mixture of dextrose, amino acids and alcohol in the parenteral feeding of more than 600 surgical patients in the course of the last two years. It has been their aim to provide parenterally the full nutritional and caloric requirements of the individual until he is able to consume food without difficulty and without discomfort.

It has become a routine with them to administer immediately after operation 1,000 cc. of fluid containing amino acids 5 per cent, glucose 5 per cent and 60 cc. of 98 per cent alcohol. This is given slowly over a period of four hours. During this period the patient usually sleeps and dozes. Morphine is rarely given and rarely required. In the late afternoon and evening another 1,000 cc. is given. Therefore, within the first 12 hours after operation the patient has received 100 gm. of amino acids, 100 gm. of dextrose and 120 cc. of alcohol; a total of 1,472 calories.

On the following morning the patient is offered food in accordance with his desires, and if enough is consumed, no further parenteral nutrition is given. If the patient does not eat well, parenteral nutrition is supplemented to the point of the calculated metabolic requirements. The authors have used this method of nutrition also to prepare poor surgical risk patients for operation.

The authors do not maintain that less well-nourished patients would not get well, but their clinical observations have convinced them that patients who are provided full nutritional requirements feel better, their wounds heal more rapidly, they suffer less discomfort, they are more easily ambulated and they experience a shorter post-operative convalescence at home than was observed in patients two years ago when this regimen had not been instituted.

The authors discuss in greater detail various aspects of their use of alcohol in post-operative parenteral feeding. They found that when alcohol is given parenterally in a caloric ratio proportionate to approximately two times the caloric demands of the patient, the blood alcohol level rises rapidly during the first hour, after which it has a tendency to level off. Thereafter, if the rate of administration is decreased to approximately one and a half times the caloric demand, the blood alcohol level remains fairly constant at 0.08 gm. per 100 cc. This blood alcohol level produces mild sedation and analgesia, reducing thereby the need for morphine.

Approximately 15 cc. of 98 per cent alcohol per hour in parenteral fluids will provide a practical clinical rate of administration for the average adult individual. A positive nitrogen balance can be attained parenterally in some instances despite a negative caloric balance if an adequate amount of nitrogen is given. A strong positive nitrogen balance can be more consistently obtained, however, when adequate calories are available from extraneous sources. A positive nitrogen balance can be more easily maintained when glucose and amino acids are supplemented with alcohol than when those two nutritional elements are given alone. These studies indicate that the readily available calories derived from alcohol have the ability to spare nitrogen and to that extent can provide energy which must otherwise be obtained from body reserves.

A solution of glucose, amino acids and alcohol supplemented with vitamins B and C can provide, parenterally, the essential elements of nutrition, i.e. carbohydrate, nitrogen, calories and vitamins. Electrolytes can be added as needed.

(Rice, C. O., Minneapolis, Minn., Orr, B., and Enquist, I.: *Annals of Surgery*, 131, 289-306, March 1950. The authors are Surgical Fellows, St. Barnabas Hospital and Surgical Resident, University of Minnesota School of Medicine.)

Follow-Up Study of Patients with Thromboangiitis Obliterans

CAMPBELL and his collaborators say that during the period from 1934 to 1948 inclusive a diagnosis of thromboangiitis obliterans (Buerger's disease) was made on 283 patients at the University of Michigan Hospital in Ann Arbor, Mich. In an attempt to evaluate the various forms of therapy which had been employed follow-up inquiries were made.

Of the total number of patients on whom the diagnosis of thromboangiitis obliterans had been made, 149 were ultimately selected on the basis that they fulfilled the accepted criteria, and had an adequate record in which sufficient data, such as a pathology report on removed tissue, was available further to substantiate the original impression. The original

diagnosis had been excluded in a large number of these patients by examination at a later date, death with autopsy analysis, etc. In some, the presence of all peripheral pulses and the absence of the usual signs and symptoms of thromboangiitis obliterans mitigated against this diagnosis.

Of the 149 selected for study, a 100 per cent follow-up analysis was achieved through a written reply to a questionnaire sent to and obtained from the patient (if living), from friends or relatives (if dead, including death certificate reports), and, in many instances, return visits to the out-patient clinic for examination and evaluation. The data recorded in each case were of such a nature as to allow a complete review of the course of the patient's disease and response to various forms of therapy prior to, during, and subsequent to study and treatment at the University Hospital.

All but two of the 149 patients were males, only one had diabetes and 20 (13.6 per cent) were Jewish. The average age of onset of the disease in the patients in this series was 34.9 years with the youngest patient giving a reliable history of onset at the age of 15 years. The oldest age of onset of symptoms was 53 years.

The signs and symptoms of arterial occlusive vascular disease were present in practically all of these patients, inasmuch as they represented a rather well-advanced group with thromboangiitis obliterans. Many of the patients had been previously hospitalized, the largest number of admissions to a hospital for a single patient being 36.

Coldness of the involved extremity was present in 126 of the 149 patients at some time in the course of their disease. Raynaud's phenomena was present in 24 cases and could be elicited by exposure to ice water in every instance. All 24 of these patients had well-established organic changes in the digits and definite evidence of occlusive arterial disease. Pain in the involved extremity was present in 143 of the 149 patients. Pain relieved by local nerve block and/or sympathetic block in most instances responded favourably to treatment.

Intermittent claudication, one of the most helpful criteria in establishing the diagnosis, was present at some time in the course of the disease in 97 of the 149 patients. Ulceration of a digit, foot, leg, or amputation stump was present in 74 instances. Frequently, the ulceration was the site of previously established gangrene or had developed following amputation of a phalanx or digit. There was an associated infection, deep or superficial in 76 instances, an ulcer being present in most but not all of these patients. Gangrene of an involved part was present at the time of admission in 45 of these patients.

Suggestive but not proved evidence of visceral involvement was present in 43 of the patients in this series. These included one renal, 17 cardiac, seven splanchnic, five ophthalmic and 13 cerebral.

Seventy-six of the 149 patients had either definite clinical signs, a history of, or pathologic confirmation of superficial migratory phlebitis. This incidence is somewhat higher than other reported series, but may merely reflect the exclusion of patients from the series in whom the diagnosis of Buerger's disease was considered doubtful. The upper extremity was the site of involvement in five patients, the lower extremities in 62, and nine patients had superficial phlebitis involving both upper and lower extremities.

Sixty-eight of the 149 patients (45.6 per cent) had had one or more amputations during the course of their illness. One patient had undergone 34 amputations and two had had 30 amputations. Investigating the years during which amputations were carried out it was found that between 1940 and 1948 only six patients required major amputations. All of these were performed in persons who were beyond the possibility of relief by conservative measures when first seen. The addition of chemotherapeutic and antibiotic agents

to the therapy has undoubtedly lessened the number of secondary amputation procedures following the removal of a phalanx or digit because of the better control of attendant infection. These agents have also prevented, in many instances, the development of gangrene secondary to infection.

Thirty-eight of the 149 patients underwent sympathectomy; 14 evidenced a very satisfactory response to their sympathectomy, and the remaining 24, a fair or poor response. Ultimately, in the course of the disease, 16 of the 38 patients lost a portion of an extremity by amputation although all of these were not necessarily related to the area previously sympathectomized. The authors feel that the decision of performing a sympathectomy in patients with thromboangiitis obliterans should be primarily related to the course of the disease; that is, the race between episodic progressive vascular occlusion on the one hand, and the development of collateral vascular channels on the other hand. The authors gained the impression that if sympathectomy is to be employed at all it should be done early in the course of the disease.

Reviewing the data on the use of tobacco, the authors say that of the 121 living patients, 88 were still using tobacco.

The authors gained the impression that psychosomatic factors are very important in thromboangiitis obliterans, both from the standpoint of etiology and of persistence of the disease. Many of the patients were frequently married and divorced, many exhibited a belligerent-bellucose type of personality with a noticeable tendency to refuse to carry out in detail the advice of the physicians they consulted. The data relevant to the use of tobacco are of interest in this respect. Several of the patients had developed drug addiction which was exceedingly difficult to control. It appeared that patients with Buerger's disease are more prone to have accidents with resultant injury to the extremities than the average individual. Many of the patients had recurrent episodes of phlebitis or further vascular occlusion while under obvious stress from environmental factors, such as difficulties at home, financial worries, lack of employment, etc.

While such features do not lend themselves readily to statistical analysis, they do represent an important series of impressions obtained from an analysis of the entire course of the disease in a carefully surveyed group of patients with Buerger's disease.

(Campbell, K. N., Harris, B. M., and Collier, F. A.: *Surgery*, 26, 1003-1013, December 1949. The authors are connected with the Department of Surgery, University of Michigan, Ann Arbor, Mich.)

The Nerve Supply to the Maxillary Incisors

(Reproduced from Dental Newsletter, No. Wa 283, dated July 1950, prepared by the American Dental Association)

THE author states that the anatomy with which the oral surgeon deals has not been completely explored and that writers have accepted the descriptions of early anatomists.

There are variations in the nerve supply to the maxillary teeth, and it was taught that they were solely innervated by the anterior superior alveolar nerve.

The author explains the anatomy in cases of bilateral cleft lip and palate, that it would be impossible for the anterior superior alveolar to reach these teeth, and that it is a known fact that these teeth

have a normal pulp sensation. The suggestion of the author that these pulps are innervated by the nasopalatine nerve is substantiated by seven reasons:

1. That these teeth have not been consistently anesthetized by injecting the anterior superior alveolar nerve alone.

2. On failure of anesthesia of these teeth by the anterior superior alveolar and on injection high in the incisive canal these teeth are anesthetized.

3. That the upper incisors are partly desensitized when the rhinologist anesthetized the nasal septum with cocaine packs.

4. The nasopalatine nerve develops on the lateral surface of the frontonasal process and that demonstrates that the nerve and the upper incisors develop together.

5. The anterior superior alveolar and nasopalatine nerves are branches of the maxillary division of the fifth cranial nerve, and have identical fibre origin and construction.

6. The nasopalatine nerve before entering the incisive canal gives anastomosing branches to the anterior superior alveolar nerve.

7. A dissection demonstrated a course by which the maxillary incisors could be innervated by the nasopalatine nerve.

The author has presented his work to anatomists, neuroanatomists and embryologists who agreed to the theory of the nasopalatine nerve sending fibres to the maxillary incisors as reasonable and probable.

(Cook, William A., Detroit, Mich.: *Journal of Oral Surgery*, April 1949.)

The following 4 items are reproduced from Medical Newsletter, Wa 280, dated July 1950, prepared by the American Medical Association:—

Observations on the Physiologic Effects of Cortisone and ACTH in Man

SPRAGUE and his associates of the Mayo Clinic point out that the dramatic alteration of the rheumatic state which follows the administration of cortisone or ACTH was reported previously by Hench and his collaborators. This report is concerned with the clinical and metabolic studies of 33 patients who received cortisone or ACTH or both for varying periods. One of the patients also received compound F. Most of the patients received the hormones for fairly prolonged periods. While more observations were made of the effects of cortisone than of ACTH, it was apparent, as expected, that the two hormones had many effects in common.

The data reported confirm what has long been known or suspected, namely, that cortisone and ACTH are powerful hormonal agents which influence a variety of physiologic processes. Many of the manifestations of Cushing's syndrome were induced by protracted administration of cortisone. The features induced in varying combinations included rounding of the facial contour, hirsutism, acne, keratosis pilaris, muscular weakness, edema, amenorrhea, cutaneous striae, mental depression, impairment of carbohydrate tolerance, negative nitrogen balance, increased excretion of corticosteroids in the urine and hypochloræmic hypopotaemic alkalosis.

In addition, metabolic studies disclosed that cortisone and ACTH increased excretion of the creatine and uric acid in the urine and gave rise to a negative balance for potassium in some cases. Their effects on balances of sodium and chloride were variable, the usual pattern

being retention of salt early in the period of administration of the hormone followed by increased excretion when administration was prolonged. In some cases there were slight increases in urinary excretion of calcium and phosphorus. Compound F in an average dose of 75 mg. daily for 12 days did not have pronounced metabolic effects.

Studies of the urinary steroids provided evidence that the adrenal cortex of man when stimulated by ACTH secretes 17-hydroxy-corticosterone (compound F) rather than cortisone. Evidence was obtained that a small percentage of administered cortisone is excreted in the urine as 17-ketosteroids and corticosteroids. Small amounts of unchanged cortisone were present in the corticosteroid fraction.

Cortisone is capable of depressing the function of the adrenal cortices in man, as it does in the rat. The authors suggest that such terms as 'side effects' or 'toxic reactions' not be applied to physiologic alterations induced by cortisone and ACTH, for these designations do not indicate a broad appreciation of the biologic significance of these important substances.

(Sprague, R. G., Rochester, Minn., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: *Archives of Internal Medicine*, 85, 199-258, February 1950. The authors are connected with the Division of Medicine; the Division of Biochemistry; the Endocrinology Laboratory, Section on Clinical Physiology and the Division of Clinical Laboratories, Mayo Clinic and Foundation, Rochester, Minn.)

Radioactive Phosphorus in Chronic Lymphatic Leukæmia

THE authors present a study of 100 cases of chronic lymphatic leukæmia treated with P32 (radioactive phosphorus). Comfortable life appears to have been prolonged as compared with the average life-span after other methods of treatment. When this report was prepared, 33 per cent of the group had lived five or more years after onset and 10 per cent eight or more years.

These figures will be extended with the passage of time, since 24 of the patients are still living. When compared with five-year end results in other types of neoplastic disease, such as carcinoma of the breast, prostate, lung, stomach and œsophagus, these results are relatively good and do not encourage the prevalent hopeless attitude taken by many doctors confronted with the problem of treating chronic leukæmia. This attitude is undesirable, since, when patients are first seen, one cannot rule out the possibility of long and comfortable life. This method of treatment is advantageous in its convenience for both patient and physician and in the lack of radiation sickness.

(Lawrence, John N., et al.: *Chronic Lymphatic Leukæmia—A Study of 100 Patients Treated with Radioactive Phosphorus. The Journal of the American Medical Association*, 140, 585-588, June 1949).

Promacatin in Treatment of Leprosy: Progress Report

JOHANSEN and his associates say that promacatin is a drug which at one time was referred to as Internal Antiseptic 307. It is a sulphone closely related chemically to promin, diasone, and sulphetrone, and is of relatively low toxicity, because it does not break

down into diaminodiphenylsulphone, which is the parent substance of promin, diasone, sulphetrone, and promacetin. This parent substance is much more toxic than any one of these derivatives. It is believed, therefore, that the degree of toxicity of the sulphone drugs depends upon the extent to which they break down in the human body into diaminodiphenylsulphone.

Studies on promacetin indicated that even with massive doses by mouth the blood level of the drug will seldom attain dangerous proportions. These features of promacetin together with evidence that it has antileprotic properties on oral administration, induced the authors to further investigate its possibilities in the treatment of leprosy.

Promacetin is sodium 4,4'-diaminodiphenylsulphone-2-acetylsulphonamide. It is a white crystalline compound soluble up to 3 per cent in water at room temperature.

The clinical material for this preliminary evaluation of promacetin included 27 patients—26 of the lepromatous, and one of the tuberculoid type.

The daily oral dose was gradually increased from 0.3 gm. daily to up to 4 gm. daily. Like the other sulphones it was given at meal-time.

Objective clinical improvement of skin and mucous membrane lesions of lepromatous leprosy occurred following the oral administration of promacetin. The improvement was uniform, universal and sustained.

Reduction in the number of leprosy bacilli in the skin and mucous membrane followed clinical improvement. Skin smears commenced to show a noticeable reduction of bacilli at the end of one year's treatment and many patients showed an absence of bacilli in the mucous membrane at this time.

Promacetin was well tolerated. Slight depression of the erythrocyte count may occur during the first few weeks of treatment, but unless other complications of the disease were present, such depressed counts usually returned to the original level spontaneously. Further blood studies are necessary.

Renewed clearing after promacetin therapy of apparently stationary residual lesions in patients previously treated with sulphones suggests that a wider application should be made of alternating or combined treatments in leprosy.

[Johansen, F. A., Erickson, P. T., Wolcott, R. R., Meyer, W. H., Gray, H. H., Prejean, B. M., and Ross, H.: *Public Health Reports*, 65, 195-207, February 1950. The authors are connected with the United States Marine Hospital (National Leprosarium), Carville, Louisiana.]

Clinical Use of the Antibiotic Chloramphenicol (Chloromycetin*)

SMADAL says that the first reports on the new antibiotic chloramphenicol (chloromycetin*) described laboratory experiments in which the antibiotic was shown to inhibit the growth *in vitro* of a wide range of bacteria and to have a chemotherapeutic effect in a number of experimental rickettsial and virus infections.

The clinical application of chloramphenicol has progressed rapidly in the past year and a half, and a wide variety of rickettsial and bacterial infections of man are now known to be controlled by the proper therapeutic use of this drug. Work carried on in Mexico and Bolivia provided good reason for the belief that chloramphenicol was of considerable value in the treatment of patients with epidemic or with murine typhus. Extensive and more definitive studies on the

related disease, scrub typhus, which were undertaken in 1948 in Malaya, clearly proved the great efficacy of chloramphenicol in controlling this rickettsial infection of man.

There are several rickettsial diseases of man which are of importance in the United States. These are Rocky Mountain spotted fever, murine typhus, Q fever and rickettsial pox. In the laboratory chloramphenicol inhibits the growth of each of the agents responsible for these diseases, and reference has already been made to its efficacy in patients with murine typhus. Information on its use in the treatment of patients with Q fever or with rickettsial pox had not been published to the time of writing.

Chloramphenicol is decidedly rickettsiostatic for all the rickettsial agents which commonly affect man, and in those human infections in which it has been employed, the results have been highly beneficial. Although therapeutic regimens for the rickettsial diseases may be modified as the result of the future work, the general schedule used at present is as follows: An initial loading dose of 3 to 4 gm. of chloramphenicol is given by mouth, and this is followed with 0.25 gm. doses every two or three hours until the temperature returns to normal levels. This schedule generally requires 5 to 10 gm. of drug over a period of one to three days. Chloramphenicol is of low toxicity.

In addition to the rickettsial disease, chloramphenicol has been shown to be of value in typhoid and brucellosis.

Although this paper is not concerned with the other new antibiotic, aureomycin, which also has proved extremely valuable in the treatment of patients with rickettsial infections, experience indicates that results with aureomycin in these human infections are entirely comparable to those obtained with chloramphenicol.

(Smadel, J. F.: *The Journal of the American Medical Association*, 142, 315-318, February 1950. The author is connected with the Department of Virus and Rickettsial Diseases, Army Medical Department, Research and Graduate School, Army Medical Centre, Washington, D.C.)

The following 5 items are reproduced from the 17th bimonthly report on Chemistry and Chemical Engineering in the United States, dated July 1950, prepared by the American Chemical Society:—

Aureomycin found to be Potent Growth Factor as well as Drug

THE discovery that the golden drug aureomycin is a potent growth accelerator, producing effects beyond those obtainable with any known vitamin, was announced in a report to the American Chemical Society's 117th national meeting.

In animal experiments which cast the antibiotic in a spectacular new rôle, and which may hold enormous long-range significance for the survival of the human race in a world of dwindling resources and expanding populations, aureomycin has increased the rate of growth of hogs by as much as 50 per cent, declared the report, submitted by Dr. E. L. R. Stokstad and Dr. T. H. Jukes of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

Although aureomycin's hitherto unsuspected nutritional powers promise to be of importance primarily in extending the world's meat supply and decreasing its production costs, they may also prove directly beneficial to human health by aiding the growth of malnourished and undersized children, the report indicated,

revealing that clinical investigations of this possibility have been launched.

Previously aureomycin, like penicillin, streptomycin, and the other antibiotic wonder drugs, was regarded solely as a weapon for fighting disease. Aureomycin has been found particularly useful against such ailments as virus pneumonia, whooping cough, Rocky Mountain spotted fever, undulant fever, typhus, eye infections, amebic dysentery, streptococcus and staphylococcus infections, and parrot fever.

The Lederle chemists stumbled upon aureomycin's growth-promoting value in the course of research on vitamin B₁₂, another powerful growth stimulator.

Chicks and turkey poults as well as pigs have registered unprecedented gains upon receiving minute quantities of the drug in the form of a finely ground powder mixed with their feed, according to the report. In fact, in the experiments conducted so far, aureomycin has been found to produce a growth response that 'cannot be duplicated by any of the vitamins known at the present time, even when added in many times the normal requirement', the report declared. No undesirable side-effects have been observed, it was said.

Aureomycin, which was first isolated about 4 years ago by Dr. B. M. Duggar of the Lederle Laboratories, and which derives its name from its golden colour, is the first antibiotic to be used to promote growth in farm animals, although laboratory tests of the nutritional value of some other antibiotics have been made, it was stated.

Just how aureomycin works in speeding growth is something Dr. Stokstad and Dr. Jukes have yet to determine, they admitted. Since other antibacterial agents with widely differing chemical structures can produce similar though less dramatic results, it seems unlikely that aureomycin functions as a vitamin, the paper explained, adding:

'It is more probable that it inhibits growth of certain detrimental micro-organisms in the intestinal tract. These bacteria may rob the intestine of some unknown vitamin, or they may produce a toxic compound.'

Aureomycin, like penicillin and streptomycin, is obtained from a mould by fermentation. Fermentation products used in the preparation of antibiotics were found to contain vitamin B₁₂, and these materials were developed as commercial sources of the animal protein factor for the feed industry. It was observed at the Lederle Laboratories that such a product prepared from the aureomycin fermentation gave a growth response with chicks which was greater than that which could be obtained with pure vitamin B₁₂, and this precipitated a coast-to-coast series of experiments which yielded the results summarized in the Stokstad-Jukes paper.

Vast Untapped Food Reserve found in Central American Plants

A vast untapped food reserve in Central America, provided by common weeds and a variety of other edible plants, has been uncovered in a 3-year survey conducted by the Nutritional Biochemistry Laboratories of the Massachusetts Institute of Technology, Cambridge, Massachusetts, the American Chemical Society was told at its 117th national meeting.

Nine hundred and thirty-seven samples representing more than 200 kinds of food from plants were collected in Honduras, Guatemala, El Salvador, Costa Rica, Nicaragua, and Panama and were analysed at the Massachusetts Institute of Technology during the survey, according to a report by Dr. Hazell E. Munsell and 5 co-workers.

The study was undertaken early in 1946, Dr. Munsell said, explaining that 'in initiating steps to improve food production in any country it is of first importance to know the potential food value of indigenous edible plants'.

The general procedure called for collection and identification of specimens by a botanist living in each area, and stabilization of a representative sample of the edible portion for shipment to the Massachusetts Institute of Technology Laboratories. The analytical work at the Institute, which was completed early this year, involved a total of 11,951 determinations, Dr. Munsell stated.

Three weeds which showed up as important potential foods, she said, were *bledo extranero*, or lambsquarters; *chipilin*; and *macuy*, or *mora*. All three gave high values for calcium, iron, the B-vitamins thiamine and riboflavin, and ascorbic acid, or vitamin C, and the first two also had sizeable contents of carotene, from which vitamin A is obtained, and niacin, another B-vitamin.

'Chaya, the leaves from an ornamental tree, is not known to be used as food in Honduras, where it was obtained, but it is edible and gave very high values for calcium, iron, carotene, riboflavin, niacin, and ascorbic acid,' Dr. Munsell continued. 'Tampala, one of the pigweeds, is used as a cooked vegetable. The sample gave high values for calcium, iron, carotene, riboflavin, niacin, and ascorbic acid.'

'Leaves of the cassava, *hojas de yuca*, may be eaten after cooking, although they are not known to be used as food. The nine samples examined gave high values for calcium, iron, thiamine, riboflavin, niacin, and ascorbic acid.'

An aquatic herb called *Jussiaea repens*, taken from the Rio Yeguaré in Honduras, is another valuable food not used at present, Dr. Munsell declared.

The growing points and tender leaves of squash and pumpkin vines are eaten commonly in Central America, . . . , she reported, adding that samples studied contained plenty of calcium, iron, carotene, thiamine, riboflavin, niacin, and ascorbic acid. Also highly prized as food are the flowers of the *yuca* plant, which are rich in thiamine, riboflavin and niacin, and particularly ascorbic acid. *Yuca* hearts also are eaten, providing valuable sources of calcium.

'Motate represents the tender edible leaf bases of a shrub used as hedges and found growing abundantly throughout Central America, although used commonly as food only in El Salvador,' she continued. 'It showed a relatively high content of calcium.'

Likewise rich in calcium are the flowers of palms, or *pacaya*, which are popular as food in Guatemala.

A Dr. Jekyll-Mr. Hyde sort of plant is the *Marva parviflora*, which is sometimes eaten in Guatemala but which can be a very troublesome weed in cultivated areas, Dr. Munsell said. The plant, a native of Europe, has a large content of calcium, iron, carotene, thiamine, riboflavin, niacin, and ascorbic acid, 'indicating that 'it might be advantageous to make more extensive use of it as food', she noted.

Among the Costa Rican plants studied, most of them from the San Jose area, were the abundant *puntas de chayote*, or growing ends of *chayote*, which proved rich in iron, carotene, thiamine, riboflavin, and niacin. Two samples of *yuca* flowers gave outstandingly high values for calcium, she said.

'Analyses were made with nineteen samples of beans, varying in size from the very tiny rice bean, *frijol de arroz*, to the large red bean, *frijol guaria*; in colour from white to blood red, and of many shapes,' she stated. 'The outstanding feature, with one or two exceptions, was their remarkable similarity in composition. The rice bean showed the greatest difference in its very high content of calcium.'

Analysis of parsley, Dr. Munsell noted, 'again focused attention on this food as a source of calcium.'

iron, thiamine, riboflavin, niacin, and ascorbic acid, indicating that it should be eaten and not used merely as decoration for some other usually less valuable food'.

Kafir corn, or maize de Guinea, is an excellent source of niacin and several other nutrients, she added, and is therefore a cereal worthy of consideration.

Every Part of a Cancer-causing Chemical can now be Traced through the Body

RADIOACTIVE techniques now permit chemists, for the first time, to trace all parts of a cancer-forming chemical through body processes, Dr. John H. Weisburger of the National Cancer Institute, Bethesda, Maryland, reported to the 117th national meeting of the American Chemical Society.

This achievement may make possible identification of the specific part of the compound which causes cancer.

Many chemical compounds which are foreign to the body are known to incite cancer in both animals and human beings, Dr. Weisburger said. These compounds are called carcinogens. Dr. Weisburger described research on the carcinogen 2-acetylaminofluorene using radioactive tracer techniques. Important points of the molecule of the carcinogen were labelled with radioactive carbon so that all the compound could be traced through an animal and thus be accounted for.

'In contrast to previous techniques, which accounted for less than a third of the cancer-inducing material and its products, the new method traced and recovered the full amount,' he said.

The experiments were carried out by administering the carcinogen to a healthy young rat by stomach tube. The test animal was kept in a 'metabolism cage' so that excretions, and even respired air, could be tested for radioactivity by the use of delicate Geiger counters. After the tests were completed, the rats were anaesthetized and killed by withdrawing blood from the heart. All important organs and tissues were dissected, and analysed for radioactivity. Simple calculations showed how much of the tagged portion of the carcinogen was present in the organ, and when total radioactivity in all parts was added up, nearly 100 per cent was recovered, Dr. Weisburger declared.

'Hence, the studies apparently gave an accurate picture of the distribution of the carcinogen or its breakdown products in rats,' he said.

It was interesting to observe that when one part of the carcinogen molecule was labelled, nearly all the radioactivity was recovered in the excretions, whereas when another part of the molecule was tagged, the expired breath of the animal became radioactive, showing that that particular part of the compound went into the formation of carbon dioxide in the body, the scientist pointed out.

Modern Air Pollution Crumbling Ancient Monuments of Greece

THE sulphur dioxide breath of the twentieth century is slowly crumbling such ancient marble monuments as those on the Acropolis of Athens, which the passing of previous centuries had left relatively untouched, Dr. A. J. Sofianopoulos of the University of Dayton, Dayton, Ohio, reported recently to the American Chemical Society.

He declared that the best way to prevent their ruin is periodic washing with pure water.

'The important clue to the principal cause of the weathering of marble monuments in Athens is found in the dark spots and areas, some black and others brown or tan, on the surface of the stone,' Dr. Sofianopoulos said. 'It was in these areas that destructive deterioration was most in evidence. The brown areas were found to be the result of oxidation of ferrous iron in the stone which caused its spontaneous detachment and fall.'

'The black spots were the result of an accumulation of dust on the surface of the stone and this coating of dust was found to be the most important factor in the deterioration of the marble. Such dust is everywhere in the air and settles even on smooth vertical surfaces, forming a firmly attached layer. This layer of dust has a porous structure and a relatively large internal surface area which permits the adsorption of considerable water from the atmosphere.'

'Deleterious gases from the atmosphere, such as sulphur dioxide which is now present in appreciable amount in all large cities such as Athens, dissolve in this adsorbed water to form acid solutions which directly attack the stone.'

'This action may not only promote the conversion of the iron in the stone from the relatively stable form of ferrous carbonate to ferric compounds, but acts directly on the calcium carbonate. Furthermore, the crystallization of the salts formed by this chemical action contributes to the deterioration of the stone. Dust that collects in crevices and joints enlarges them and ultimately may cause the detachment of pieces of stone of considerable size. Unfortunately, this dust, because of its composition, remains largely unaffected by this chemical action and tends to accumulate continuously.'

'The real remedy for this deterioration of marble by dust is to prevent its accumulation on the surface of the stone. The best and most practical means of conservation is to wash down the marble periodically with pure water so as to remove the dust before it causes any damage.'

Doubling Human Life-Span in Next 10 Years Possible, Chemist Says

THE human life-span might be doubled within the next 10 years if a \$3,000,000 fund could be obtained to finance research in the field known as gerontotherapeutics, Dr. Thomas S. Gardner of Hoffmann-La Roche, Inc., Nutley, New Jersey, told a meeting of the American Chemical Society.

Gerontotherapeutics, Dr. Gardner said, is that branch of science concerned with slowing down the aging rate and preventing the development of many, or most, of the ailments of the aging and aged. It is the 'final approach to a solution of the problem' of lengthening the life-span, the speaker said.

There are four types of research on aging, Dr. Gardner explained. One, geriatrics, deals with the treatment of diseases of the aged. A second seeks the psychological adjustment of the aged. Both of these fields are important, but neither offers any hope of a prolonged or healthier life-span, Dr. Gardner pointed out, asserting that 'at best they are crutches'. A third kind of research, gerontology, investigates the biology of aging, and provides the foundation for the practical development and application to human beings of the new science of gerontotherapeutics.

'Funds have been obtained for geriatrics, psychological adjustment of the aged, and gerontology,' Dr. Gardner said. 'However, funds are lacking for the final stage, gerontotherapeutics.'

'Careful estimates indicate that as little as \$3,000,000 under competent supervision over a period of only about ten years offers positive hope of doubling the human life-span. Unfortunately, to date funds for this final phase have been lacking. Work in geronto-therapeutics should begin now so that ten years from now a partial solution to the problem of aging can be used by the general public and medical profession. The big problem is to get the \$3,000,000 to do this work.'

Chlorguanide Hydrochloride and Malaria

(From the *Journal of the American Medical Association*, Vol. 142, 11th March, 1950, p. 745)

Dr. DE ROOK, chief of the medical service of the New Guinea Oil Company, tested the prophylactic action of chlorguanide hydrochloride (proguanil) against malaria in about 500 prisoners in a government jail 4 miles from the west point of New Guinea. The prisoners represent a fairly homogeneous group, more than 90 per cent of them originating from South Celebes and all having been exposed to malaria organisms in a highly infected lowland of New Guinea for thirteen to twenty-one months. The drug, 100 mg. twice weekly, was given for three months to about 211 prisoners, the remaining 260 serving as controls. The results were satisfactory; the spleen index decreased from 38 to 8 per cent and *Plasmodium falciparum* disappeared from the blood. Dr. de Rook, in his article in *Documenta Neerlandica de Morbis Tropics* (1, 160, June 1949), stresses this last point. The daily ingestion of 0.4 to 0.6 gm. of quinine reduces also the number of fever attacks, but the 'break-through' in New Guinea is nearly always caused by *falciparum* organisms. When using chlorguanide hydrochloride he found the reverse to be the case; the majority of the few attacks he observed were caused by *Plasmodium vivax*. Since most authorities ascribe the outbreak of blackwater fever to repeated infections with *P. falciparum* and since blackwater fever was well known in earlier settlements of New Guinea, the author believes that the use of chlorguanide hydrochloride offers new prospects for this island.

Chloramphenicol in Typhoid Fevers

By M. J. SHAH

(Abstracted from the *Indian Journal of Medical Sciences*, Vol. 4, June 1950, p. 250)

CHLORAMPHENICOL has high therapeutic value in typhoid fevers.

Typhoid cases, early in their course up to the tenth day, show maximum benefit in recovery and shortening of illness.

Typhoid cases, if treated by the drug late after the tenth day, benefit as regards the shortening of illness, but there is no appreciable advantage in incidence of recovery, relapse and mortality.

In typhoid fevers, chloramphenicol in half dosage with an average total of twelve grammes gives the same therapeutic results as in full doses with an average total of twenty-one grammes.

Incidence of toxic effects is reduced in half dosage.

In treatment of typhoid fevers, the author recommends a new dosage schedule, which is economic and equally effective.

Thoracic Amoebiasis

By A. S. BOOKLESS

(Abstracted from the *Journal of the Royal Army Medical Corps*, Vol. 94, February 1950, p. 52)

WARTIME experience led one to respect amoebic liver infection as a potentially insidious condition especially when masquerading an acute thoracic disease.

Evidence of disease in the right chest was found in 10 out of 26 patients suffering from hepatic amoebiasis in Middle East hospitals, but realization of its significance was often delayed.

In spite of the many original papers on this subject, textbooks still emphasize the relatively common lung abscess and barely mention these atypical syndromes, which are consequently too often regarded as side-effects or late complications rather than predominating features.

For these reasons a detailed account of some of our patients should be profitable.

Ten out of 26 patients with hepatic amoebiasis had lesions in the right chest. Yet not a single lung abscess was found.

Amoebic hepatitis was the commoner underlying condition compared with liver abscess.

Signs and symptoms of chest disease were often acute, and preceded those of the associated liver condition.

Right shoulder pain received insufficient attention.

These chest lesions may not always be due to the actual entry of amoebae into the thorax.

The consideration of pulmonary amoebiasis in the differential diagnosis of right-sided chest disease is advocated.

Gantrisin in the Treatment of Urinary Infections

By G. CARROLL *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. 142, 14th January, 1950, p. 85)

THIS report describes our experience in the evaluation of a new sulphonamide drug, gantrisin (3,4-dimethyl-5-sulphanilamido-isoxazole).

Our studies *in vitro* on 131 strains of various organisms indicated the following degrees of sensitivity to gantrisin; the organisms are listed in the order of their decreasing sensitivity: *Proteus*, *Alcaligenes*, *Escherichia coli*, *paracolon bacillus*, *Escherichia intermedium*, *Aerobacter aerogenes*, *Streptococcus faecalis* and *Pseudomonas*.

These studies *in vitro* consistently demonstrated that *Proteus* was highly sensitive to gantrisin.

Pseudomonas proved to be the least sensitive of all the organisms tested with gantrisin.

In vivo the dosage used at first was 1 gm. of gantrisin every six hours for twenty-four hours. Encouraged by the absence of toxic symptoms we later increased the dose to 2 gm. every six hours. The patients received no concomitant alkali, and no special effort was made to force fluids, although records were kept of fluid intake and output. A few patients who were too ill to tolerate oral medication were given gantrisin intramuscularly or intravenously. This was facilitated by the high solubility of the drug, which permitted the use of a solution containing a 40 per cent concentration of gantrisin.

Our entire experience with this drug has been characterized by the absence of toxic symptoms.

We are of opinion that gantrisin is the drug of choice in the treatment of Proteus infections.

Cooley's Anæmia

By N. K. CHANDRA AND OTHER

(Abstracted from the *Indian Journal of Pediatrics*, Vol. 18, April 1950, p. 89)

Four cases of Cooley's anemia are reported below with a view to draw attention to its incidence in India. Hitherto only five cases are reported in Indian medical literature. It was believed that the disease occurs only in Mediterranean races. But its incidence in Indian people shows that it is not confined to any racial group. All the four cases reported here have been seen within a period of 18 months in Calcutta. If a wider search is made many cases, which are diagnosed as unknown splenomegaly, may be found to be Cooley's anemia. As a matter of fact, the cases reported were sent to us with a diagnosis of kala-azar. (Here follows description of 4 cases.)

The disease may appear at any time of the first decade of life. The initial manifestations are so mild in nature that medical advice is not sought for until the child is two to three years of age or older. The malady occurs with equal frequency in both sexes.

The onset of the condition is gradual. The earliest manifestation that attracts attention of the parents is pallor. Early in the disease the spleen is enlarged and the liver becomes palpable. The colour of the skin becomes muddy. With pallor and progressive protuberance of the abdomen, there is increasing weakness and general malaise. Bouts of rise of temperature are not uncommon. Some parents may come with the complaint of enlargement of the head of the child. The growth is retarded, but mentally the patients are normal. The facies usually is mongoloid, indicated by high malar bones, prominent eyes with an epicanthal fold and a short nose with a depressed bridge. The prominence of abdomen is often a striking feature. In some cases the enlargement of peripheral lymph glands without any tenderness has been noted. The blood examination reveals microcytic hypochromic anemia. Urine usually contains excess of urobilin and urobilinogen. Bone marrow puncture reveals increase of cellular element indicating the hyperactive state.

Röntgenological finding of the bones, specially of the skull and of the hands and feet, are very characteristic. The diploic space is widened and vertical striations at right angles to the inner table are marked producing 'hair-on-end' appearance. The outer table in some cases may be absent. The bones of the hands and feet show typical mosaic appearance.

The patients in whom the disease develops early very seldom live beyond the tenth year. More chronic cases die of intercurrent infection while rapidly deteriorating cases die of anæmic state with enlarged heart. Mild cases, however, do exist which may be overlooked.

The treatment of Cooley's anemia is extremely unsatisfactory as it is purely symptomatic.

Pain in the Chest Wall simulating Heart Disease

By D. R. ALLISON

(Abstracted from the *British Medical Journal*, i, 11th February, 1950, p. 332)

PAIN in the chest offers a wide field in differential diagnosis, and is particularly interesting to the clinician, because in the majority of cases simple clinical methods

are sufficient to establish its origin and nature. In spite of this, mistakes are frequent, and 10 per cent of patients referred to hospital with a diagnosis of angina are found in fact to be suffering from pain arising in the chest wall only, with no evidence whatever of underlying cardiac disease.

The frequency with which such patients are seen in routine out-patient work, emphasizes the need for an orientation towards pain in the chest, and suggests that in clinical teaching pride of place is too often given to angina pectoris in explanation of the pain and too little regard is paid to local structural causes.

This paper is based on a follow-up of 50 consecutive cases to which a diagnosis of coronary disease had been wrongfully applied, and in each case the cause of the pain was found to be in the structures of the chest wall. It takes no account of the many cases in which coronary disease is simulated by visceral disease elsewhere or is an expression of an underlying anxiety neurosis.

In almost all the cases the mistake in diagnosis had been due to the readiness with which precordial pain on effort had been accepted as indicating heart disease without realizing the need for the closest questioning on the time relationship between the effort and the pain and the exact nature of the effort involved.

The cases under review were classified as follows: (1) muscle strain affecting the chest wall and attachments of the diaphragm, 16 cases; (2) fibrositis of the chest wall, 20 cases; (3) kyphoscoliosis and osteoarthritis of spine, 14 cases.

A detailed history is of paramount importance in all these cases, and due regard should be paid to a family history of coronary thrombosis. The exact conditions in which the pain occurs should be checked and counter-checked, and the time relations of the pain should be ascertained. The factors which bring relief must also be considered, and, in particular, relief from change of posture is important.

Relief from trinitrin should not be accepted without inquiry about the interval before relief is obtained, as this is sometimes half an hour or more, or in any case too long for a drug to be really responsible for the improvement.

Pain induced by excitement and anger is most unlikely to be of chest-wall origin, and this is therefore a most important differential point.

Pain arising in the chest wall has certain characteristic features, the most important of which is local tenderness, particularly in fibrositic cases. In these cases the tenderness is well localized, sometimes to small discrete areas which can best be felt with the finger-tips. These tender spots may be on the surface of the ribs or sternum or may be in the intercostal spaces, and the pain elicited is acute when the exact spot is found.

The second characteristic of pain arising in the chest wall is related to movement. This is especially pronounced in those pains associated with muscle strain and fibrositis. The pain is made worse on initiating movement before any real exertion is involved, and it may be made worse by turning in bed or on reaching towards a bedside table.

The question whether a patient's pain is made worse on turning in bed is probably the most important question to ask in these cases of chest-wall pain simulating coronary disease. A patient with acute coronary infarction may find that turning in bed is painful, but it is more the change of posture than the actual initiating movement of turning which causes the increased pain; many patients state that their pain comes on in bed when they really mean that it comes on when turning in bed.

Chest-wall pain, though usually related to specific movement, may be increased on general exertion if this involves increased respiratory effort. True anginal

pain is usually felt long before there is sufficient dyspnoea to increase respiratory movements.

Pain associated with kyphoscoliosis is often made worse by certain postures in bed, and patients with such a condition may wake up with pain suggesting a coronary lesion as the result of lying in some awkward position. Clinical examination, however, is usually sufficient to differentiate these cases.

The third most important point about chest-wall pain is the possibility of reproducing the pain by particular movements of the trunk against resistance. This is true particularly of pain arising as the result of muscle strain, but a detailed history will usually relate the onset of pain to some specific exertion in the past.

In spite of a detailed history and careful clinical examination there remain some cases of pain referred to the chest wall in which the diagnosis will remain in doubt, and only full electrocardiographic examination before and after exertion will serve to make the position clear.

In elderly patients who have a doubtful chest pain and some arteriopathy no serious harm is done by reasonable limitation of activity on general grounds, but cases in the younger age group demand a more accurate diagnosis, and if after complete investigation there remains some doubt, it is much better that the heart should be passed as normal.

Follow-up Observations on the Treatment of Bancroftian Filariasis with Hetrazan in British Guiana

By R. HEWITT *et al.*

(Abstracted from the *American Journal of Tropical Medicine*, Vol. 30, March 1950, p. 217)

PRELIMINARY results of the oral administration of hetrazan to 296 Guianese patients infected with *Wuchereria bancrofti* have been published. It was shown that circulating microfilariae disappeared rapidly during treatment, and that low or negative counts were sustained for from 2 to 4 months after treatment. Clinical improvement occurred during treatment in many patients who exhibited pre-treatment filarial symptoms. Monthly follow-up observations have now been made on many of these patients for periods up to 14 months after cessation of treatment, and the results of these observations form the subject of this paper.

Negative microfilarial counts were maintained in 53 out of 83 patients (63.9 per cent) for 14 months, and with few exceptions the remainder exhibited counts far below the original. The reduction in total microfilariaemia within the entire group was greater than 90 per cent, including all dose ranges of hetrazan. With the exception of total doses less than 50 mg. per kg. no significant relationship could be determined between the amount of hetrazan administered and the presence or absence of microfilariae during the follow-up period. The greatest number of recurrences occurred at the 6th month follow-up examination and declined thereafter. No new recurrences of small numbers of circulating microfilariae occurred during the 12th, 13th or 14th month.

Clinical symptoms after treatment varied considerably. Some patients who showed complete or partial relief from pre-treatment during therapy remained free of symptoms throughout the follow-up period and are apparently cured. Others revealed recurrences of pre-treatment symptoms with various degrees of frequency after treatment.

The number of microfilariae present after treatment seemed to bear no relationship to the presence or absence of symptoms after treatment.

It is believed that the sustained absence of microfilariae in a large proportion of the patients treated, together with the complete absence of symptoms after treatment in many cases, demonstrates indirectly that mature worms are permanently affected by treatment with hetrazan.

Reviews

A TREATISE ON TROPICAL THERAPEUTICS.—By Sir R. N. Chopra, B. Mukerji, and I. C. Chopra. Published by U. N. Dhur and Sons Ltd., Calcutta. Pp. xi plus 705. Price, Rs. 25; 2 guineas (In Great Britain)

THE second edition of Sir Ram Nath Chopra's well-known book on tropical therapeutics has appeared in a new garb and with Dr. B. Mukerji and Dr. I. C. Chopra as joint authors. This is the first volume of the book and it is intended to include an addendum giving newer advances when the second volume is ready.

The present volume is divided into four parts: 1. General considerations in therapy. 2. Remedies used against helminthic diseases. 3. Remedies used against protozoal diseases. 4. Remedies used against bacterial diseases. This list of course does not give an adequate idea of the contents, for included in various chapters one will find such subjects as climate and weather, vitamins and diets, nutritional and metabolic diseases, sera and vaccines, sulphonamides and antibiotics. The book has been extensively revised and some new chapters and sections added so that it may be regarded as almost a new book. As many of our readers may know the book is not only an exposition of tropical therapeutics, but includes clinical aspects of diseases so that a better understanding of the rationale of treatment may be obtained. This edition maintains the reputation of the book. Every medical library should possess a copy of this book, and practitioners will find in it many useful informations.

R. N. C.

THE RHEUMATIC DISEASES.—By G. D. Kersley, M.A., M.D. (Cantab.), F.R.C.P. (Lond.), T.D., with a Foreword by Sir Francis R. Fraser, M.A., M.D. (Ed.), F.R.C.P. (Lond.). Third Edition. 1950. Published by Messrs. William Heinemann (Medical Books) Ltd., London. Pp. xiii plus 143, with illustrations. Price, 15s. net

IN this little book the author has given accounts which are more or less common to acute or subacute rheumatism, rheumatoid arthritis, climacteric arthritis, osteoarthritis, spondylitis and gout. All these are collagen diseases in spite of a difference in minor details. This view has been supported recently by the use of ACTH and cortisone. The support is depicted in figure 7, opposite page 17.

Allied conditions like gonococcal rheumatism and arthritis, Still's disease, fibrositis and sciatica are also included.

In fibrositis the part played by psychological factors is not ignored.

A full appraisal is made of spa treatment, including the ordinary benefit the patient is likely to derive from the local specialist who naturally sees more cases than the patient's own medical adviser.

Eradication of focal sepsis is duly gone into; vaccines from extracted teeth, made with special care, may be used. Dead teeth are a problem.

A very useful publication.

S. D. S. G.

A SHORT TEXTBOOK OF RADIOTHERAPY FOR TECHNICIANS AND STUDENTS WITH A SUPPLEMENTARY CHAPTER FOR THE DERMATOLOGIST.—By J. Walter, M.A., B.M. (Oxf.), M.R.C.P. (Lond.), D.M.R.E. (Cantab.), and H. Miller, M.A., Ph.D. (Cantab.), F.Inst.P. Foreword by J. L. A. Grout, M.C., F.R.C.S. (Ed.), F.F.R., D.M.R.E. 1950. Published by J. and A. Churchill Ltd., 104, Gloucester Place, W.1, London. Pp. xii plus 444, with 199 illustrations. Price, 28s.

This book is admittedly worked up from lecture notes from lecture courses given to students working for the examination of M.S.R. and C.T. This defines its scope; and as such it is an excellent little treatise on radiotherapy and all its allied subjects.

An interesting feature is the inclusion of a chapter on dermatology. This contains much useful information, both for radiologists and skin specialists. Stress is laid on the effects of back-scatter in increasing dosage; and in the case of the hands and feet, the exit dose is usually of the order of 40 per cent so that 100r given back and front at the usual K.V. would be equivalent to 140r.

Another chapter is devoted to non-malignant cases, e.g. tuberculosis, boils, rheumatism, spondylitis, various skin conditions, warts, keloids, angioma, ringworm of the scalp, and endocrine conditions such as menorrhagia.

The body of the book deals with such subjects as: (1) The structure of matter. (2) The physical properties of x-rays. (3) Etc., etc.

On the whole it appears an excellent introduction to an ever expanding subject. Most of the statements will bear critical scientific scrutiny. The style is clear, easy to understand, even for the uninitiated. It should prove of outstanding value, not only to technicians and students, but to those practising any branch of radiology to prevent them forgetting the elementary stepping stones to the heights they have achieved.

J. A. S.

THE EXAMINATION OF WATERS AND WATER SUPPLIES (THRESH, BEAK AND SUCKLING).—

By Edwin Windle Taylor, M.A., M.D., B.Ch. (Cantab.), M.R.C.S., L.R.C.P., D.P.H. (Lond.). Sixth Edition. 1949. Published by J. and A. Churchill Ltd., 104, Gloucester Place, London, W.1. Pp. xii plus 819, with 52 illustrations. Price, 70s.

The sixth edition of this excellent book embodies many technical advances in the methods of examination and treatment of water that have been developed since the publication of the fifth edition in 1943. These have been skilfully woven in without materially altering the sound basic concepts or the language of the original text.

Taylor's contribution consists in the rearrangement of the chapters and in the rewriting of several chapters. It is refreshing to find analytical results being expressed in parts per million, in conformity with American and Continental practice. The value of the test for Biochemical Oxygen Demand is recognized more adequately. In the chapter on Chlorination, Fair's explanation of the action of chlorine in the light of dissociation of HOCl at various pH values is discussed. The orthotolidine-arsenic test has been mentioned. The process of producing de-ionized water has been mentioned. The value of microscopic examination of water in interpretation of analysis has

been dealt with. The value of the test for electrical conductivity has been emphasized. The chapters on bacteriological examination and the relation between water and disease have been revised and amplified.

The chapter on American practice and American standards is a valuable addition.

Though the author has revised the chapters on gathering grounds, underground water supplies and water treatment, his presentation of hydrological and engineering aspects is somewhat brief and inadequate from the point of view of the waterworks engineer. However, the discussion on the performance of micro-strainers is useful.

K. S.

BLOOD TRANSFUSION.—By Elmor L. De Gwinn, M.D., Robert C. Hardin, M.D., and John B. Alsever, M.D. 1949. Published by W. B. Saunders Company, Philadelphia and London. Pp. xii plus 587. Illustrated. Price, 45s.

In this book the authors have given their experience in 'somewhat immodest details' in the hope that the reader will apply the results to solve his problems. The details do solve many problems that existed at the time the book was written and indicate the lines for solving others that have arisen since.

The A-B-O blood groups are introduced in the fourth chapter, after the historical background, therapeutic choice of blood, etc., and clinical aspect of shock have been dealt with in the first three chapters. Then follow M-N, P and Rh-Hr. All this is discussed systematically, including anthropological and genetical aspects.

The laboratory procedures are introduced in the ninth chapter, after general considerations and equipment. A diagram gives the appearance of isohemagglutination. The actual handling of the begins on page 137. The descriptions are aided by sketches of racks, centrifuges, flasks, test-tubes and bleeding finger tips dropping blood into saline to make the rbc suspension. Standards of anti-A and anti-B sera as accepted in the U.S.A. are given in the general considerations.

In the tenth chapter are given the blood transfusions, donor, recipient and blood bank. Among accidents to the donor are mentioned 'Delayed syncope' occurring several hours after bleeding and 'Epidemic fainting' occurring among the donors waiting together in a room to give blood.

Agglutinating titre of the 'Dangerous Universal Donor' is fixed at 1/600 by one standard and at 1/200 by another. A previous and stricter standard by De Baker (incidentally, the first worker referred to in the book) has not been mentioned. Placental blood has not been recommended. Dangers of overloading the heart and measures for dealing with the overload have been described in detail. All details for running blood banks on a large scale and drying plasma (or serum) are available and so is information on by-products of a blood bank and plasma substitutes for intravenous alimentation.

For essential details of grouping, typing, Rh grouping, Rh typing and cross-matching of bloods and of the testing sera used, however, the beginner will not find the arrangement very easy. The first eight chapters he will appreciate only after going through what follows.

The authors do not claim to have read all the papers published on blood group, etc., 'more than 10,000'. Their selections given at the end of each chapter, however, are very helpful to the worker.

The get-up is very good. No printer's errors attract attention.

A very useful publication.

S. D. S. G.

GERIATRIC MEDICINE. THE CARE OF THE AGING AND THE AGED.—Edited by E. J. Stieglitz, M.S., M.D., F.A.C.P. Second Edition. 1949. Published by W. B. Saunders Company, Philadelphia and London. Pp. xvii plus 773. Illustrated. Price, 60s.

THERE are more aging and aged people in the world to-day than ever before in human history. If they are healthy they will be no burden to the society but assets in matters of experience, skill and judgment. Longevity can be and should be freed from senility.

This is the main object of geriatric medicine. Simple care of the aged, the senile and the infirm is a secondary object. Unfortunately, the books on traditional teaching of medicine deal with the secondary object mostly if not solely, so far as the needs of the aging and the aged are concerned. This book deals with the main object.

Here are some samples : (1) Gradual gain in weight though common is not normal. Any gain over the normal at the age of 25 has an adverse effect on health and longevity. Modern tables for height and weight do not make a concession for age—p. 36. A picture shows the difference between the lean and the fat at the successive posts on the road of life. Against 3 lean men approaching the post marked 80 there is only 1 fat man—p. 220. (2) There is no such thing as a primary endocrine obesity—p. 66. (3) Asthma appears to be a non-specific reaction in the elderly. The value of the vaccine is nil. Infection is often the trigger which sets off the attack—p. 319. (4) In cardiovascular abnormalities more can be done for the aging than for the aged, between the critical years 40 to 60—p. 486. (5) Coronary vascular disease may date from trauma to the chest wall and strain of lifting a heavy load—p. 422. (6) Legal responsibility of the senile is obscure : Unless an aged person can be said to be insane he is not ordinarily excused for crime—p. 181. (7) Pseudo-fractures may look like real fractures in a skiagram—p. 700. (8) With gentle consideration and sensible care of the aging skin much may be done to prevent serious and alleviate the annoying thousand natural shocks that flesh is heir to—p. 741. The reader will find many more items and points of view to help him in treating the elders of his generation.

No less than 47 contributors have stated their views in 44 chapters in this comprehensive book. The editor has eliminated overlapping and reduced separation of connected items to a minimum.

The get-up is very good. No printing errors attract attention.

An excellent publication.

S. D. S. G.

BOOKS RECEIVED

1. Journal of the Philippine Pharmaceutical Association. Vol. XXXVII, No. 7, 15th July, 1950. Address : 835, San Fernando, Binondo, Manila. Subscription rates : P.10.00 yearly; P.1.00 per copy.

2. International Medical Abstracts and Reviews. Vol. 8, Nos. 3 and 4, September-October 1950. Founded and Edited by : Jyoti Dhar, B.Sc., M.B. Publishing Address : Alipore, Post Box No. 5, Calcutta 27. Single copy : Rs. 2. Annual subscription : Rs. 12.

3. Premier Medical Review. Edited by Dr. G. V. Hanumantha Rao, L.O., L.M.P. (Mad.), L.C.P.S. (Bom.), Guntur. Vol. 11, No. 4, October-December 1950. Publishing Office : 4th Street, Brodiepet, Guntur

(S. India). Subscription : Annual Rs. 3-8-0. Foreign Rs. 5-8-0. Single copy Re. 1 in advance.

4. Compost Bulletin. Vol. 3, No. 2, June 1950. Issued by the Director of Compost, Ministry of Agriculture, Government of India, New Delhi.

5. Composting of Farm and Village Wastes in India. By Dr. C. N. Acharya. Printed at the Job Press Ltd., Kanpur.

6. The Indian Dental Review. Vol. XIX, No. 9, September 1950. Editor : Mansookh K. Patel, D.D.S. (Penn., U.S.A.), Dr. med. dent. (Germany), F.I.C.D. Address : 121, Esplanade Road, Fort, Bombay.

7. British Book News. No 121, September 1950. Published for the British Council by the National Book League, London. Price, 1s. 3d.

8. Britain To-day. No. 175, November 1950. Address : The British Council, 3, Hanover, London, W.1. Price, 1s. Annual subscription rate : 13s. sterling, post free.

9. Anais Da Faculdade De Medicina De Porto Alegre. Janeiro-Dezembro, 1949. Biblioteca, Faculdade de Medicina de Porto Alegre, Caixa Postal 657, Porto Alegre-Rio Grande do sul, Brasil.

10. Nuclear Science Abstracts. Vol. 4, No. 7, 15th April, 1950. Technical Information Division, ORE, Oak Ridge, Tennessee, U.S.A. Price, 25 cents.

Abstracts from Reports

THE THIRTY-SECOND ANNUAL REPORT OF KING EDWARD VII MEMORIAL PASTEUR INSTITUTE AND MEDICAL RESEARCH INSTITUTE, SHILLONG, FOR THE YEAR ENDING 31ST DECEMBER, 1948. PRINTED AT THE ASSAM GOVERNMENT PRESS, SHILLONG. PRICE, RE. 1 OR 1s. 6d.

ANTIRABIC SECTION

THE year started with 66 antirabic treatment centres with the deletion of 7 such centres which fell in East Bengal, Pakistan. During the year 10 public centres were opened bringing the total to 76, of which 31 are public centres and 45 private centres.

The total number of persons who applied for treatment during the year amounted to 3,472. Of these, 508 applied at the Shillong centre at the Pasteur Institute.

Treatment was completed in the case of 2,821 persons.

Among those that did not complete their treatment were 362 who absconded before completion of their treatment and 289 'advice' cases.

Seven deaths from hydrophobia were reported among the fully treated persons, giving a mortality rate of 0.25 per cent. This is lower than the last year's figure of 0.32 or the average of the last 32 years of 0.66 per cent.

Two had been bitten by the jackal, but the actual cause of death in one of them is in doubt; the person, a female, developed fever after a rigor on the fifth day after confinement and died two days later without taking either water or food, but she is stated to have 'feared water and fire'. The remaining five cases had been bitten by the dog. The treatment was inadequate in one of them, class II instead of class III being given.

Prophylactic cholera and T.A.B. vaccines were issued during the year as usual.

During the year 236,170 ampoules of 2 cc. each of combined cholera and dysentery bacteriophage were issued.

Small quantities of typhoid phage, type phages, phage-resistant cultures, phage-sensitive strains, as well as other stock cultures, were supplied to manufacturing concerns and laboratories.

IV. Enquiry on Naga sore (Indian Research Fund Association) under Dr. S. R. Pandit

The enquiry on Naga sore was considerably handicapped owing to its very low incidence this year and the difficulty in securing cases for investigation.

V. General Laboratory Examinations

The number of laboratory examinations carried out during the year amounted to 11,251; this is an increase by 976 over last year's figure of 10,278.

An uncommon and high mortality in rats was a subject of investigation. A large scale migration of rats from the foot hills into the adjoining tea garden areas in Lokra and Bahipara followed by a heavy death rate amongst rats was reported by the Civil Surgeon, Darrang. It would appear that the Subansiri area of North Lakhimpur subdivision had a similar experience a month previously and the migration and subsequent deaths on a large scale among rats was connected in some way with the cyclical flowering of a species of bamboo. Although sporadic flowering occurs in all seasons, flowering en masse is said to be cyclical, occurring once in 25 to 40 years, and on these rare occasions rats are attracted to the bamboo seeds on which they feed voraciously. There was no report of any case of plague among human beings. An investigation was immediately started. It was concluded from all the evidence available that whatever the cause of the epizootic might be, it was certainly not plague.

ANNUAL REPORT OF THE CHEMICAL EXAMINER'S DEPARTMENT, MADRAS, FOR THE YEAR 1949. PRINTED BY THE SUPER-INTENDENT, GOVERNMENT PRESS, MADRAS, 1950. PRICE, 6 ANNAS

DR. P. VENKAT RAO, Chemical Examiner, Madras, in his report on the working of the department during 1949 records that 10,644 articles were examined in the investigation of 2,172 cases as compared with 9,986 articles in 2,054 cases in 1948. There were 688 cases of human poisoning; poisons were detected in 277 cases, the commonest of them being oleander, nitrite, alcohol, opium, copper and *dhatūra*. There were 41 cases of animal poisoning with detection of the poison in 21 cases; arsenic was by far the most common poison.

One thousand and twenty were 'stain cases'. In 914 cases examined for blood, blood was detected in 871 cases. In 106 cases examined for semen, with or without blood, the detections were semen in 27 cases, blood and semen in 11 cases and blood in only 20 cases. There were 247 cases in the miscellaneous medico-legal group and 176 articles were sent for general analysis comprising mainly of inks.

A selection of cases of interest are cited in each group.

K. V. V.

Correspondence

[We are pleased to see this section growing in volume. Small excisions are occasionally undertaken by us to keep the tone of the correspondence dignified; no argument is omitted.]

TREATMENT OF INFANTILE CIRRHOSIS OF THE LIVER

SIR.—Will you please be kind enough to clarify the following points:—

Dr. P. Krishna Rao, M.Sc., M.B., B.S., has written in the *J.M.G.* of April 1950, for the treatment of infantile cirrhosis of liver:

Cow's milk is one of the causes of infantile cirrhosis because it lacks 'choline'.

He advises Cow & Gate (proprietary milk food). In my opinion majority of proprietary milk foods are prepared from cow's milk, if cow's milk lacks in choline how can proprietary milk foods supply choline.

The cow's milk contain 120 mg. of choline in 100 grammes of milk.*

Yours faithfully,
THAKAR SINGH, M.B., B.S.

HASANGANJ DISPENSARY,
DIST. UNAO.

*The physiological bases of medical practice by Best & Taylor.

[The sentence in the text runs as follows: 'Cow's milk evidently is lacking in certain essential food factors, especially choline and renders the liver vulnerable to infection' (page 152—*J.M.G.*, April 1950).

The word 'Lack' means both 'to be without' or 'poorly supplied with' and it is used in the text to signify the latter meaning.

It is a common knowledge that proprietary milk foods are prepared from cow's milk (they are called milk foods) and that it contains certain amount of choline. I have also mentioned in my paper that according to Bicknell and Prescott, milk contains 107 mg. of choline per 100 gm. and yet they consider that milk is not a good source of choline (page 152).

My investigations have revealed the following important observations:

- (i) All cases of cirrhotic children were those that were fed on cow's milk and belonged to the vegetarian family.
- (ii) All those children that were fed on proprietary milk food (supplemented with vitamin B complex) did not suffer from cirrhosis.
- (iii) Even those children that belonged to the so-called 'infantile cirrhosis family' escaped from this disease when fed on proprietary milk food and vitamin B complex.

Therefore, the natural conclusion is that cow's milk in this part of India is 'lacking' in even that quantity of choline as could be supplied from proprietary milk food.

It cannot be denied that cows reared by the various firms that prepare these milk foods are brought up with utmost care and in ideal hygienic conditions and the milk yielded by them is rich in all those food

factors that should naturally be present therein. Analysis of milk is carried out at various stages of preparation, and finally when it is converted into powder form deficiencies in food factors, if any, are all made up by adding those substances. Moreover vitamins and certain mineral substances are also added to these proprietary milk foods, which are very useful for the children. Under these circumstances I need hardly say that milk foods are far better suited for these children than cow's milk that is obtainable in this part of India.

The following are the reasons I attribute as to why proprietary milk foods are advocated to be better and more useful to the children than cow's milk itself :

- (i) Our cow's milk is deficient in protein as compared with the milk of western cows.
- (ii) The way in which the milk is handled, over boiled and preserved at home (at any rate in this part of India) will all tend to lower the vitamin content of the milk. Milk is not a good source of choline although it contains about 107 mg. per 100 gm. I am of the opinion that the choline content of the milk of our cows must be even lower than this. (I give this part of the reply, of course, without any data on the analysis of milk of our cows for choline content. It is a pity that choline content has not been found out here yet.)
- (iii) Proprietary milk food is prepared with utmost care and in ideal hygienic conditions. The cows are also brought up under ideal conditions to yield milk of the highest quality. Milk is pasteurized, dehydrated and analysed at various stages of preparation and finally when it is converted into powder form deficiencies in food factors, if any, are made up by adding those substances. Vitamins and certain mineral substances are also added. Therefore these milk foods supply all the necessary food factors essential for the nourishment of a child.
- (iv) These milk foods are easily digested by the children. Probably on account of a better manner of curdling.

Children get, in the week a fresh form, because at each feed it is freshly prepared.

These I consider as some of the reasons why proprietary milk foods are found to be superior to that of cow's milk as such.

P. KRISHNA RAO.]

SIR,—In the April issue of the *I.M.G.* an article is published on the treatment of Infantile Cirrhosis of the Liver by Dr. P. Krishna Rao without any comments. My own experience differs from the views expressed by the author about the causes and treatment of the disease. I request you to kindly clear my doubts either through the columns of the *I.M.G.* or personally to me.

1. In the article mentioned it is stated that (1) Cow's milk and (2) *Bacilli coli* infection are the two factors which bring about the disease and that one of the proprietary milk foods as Glaxo is the treatment of the disease. The cow's milk is avoided.

This disease is also prevalent in the Northern Circars of the Madras Province where I have been practising for the last 25 years. I find infantile cirrhosis in children fed on cow's milk, on proprietary milk foods as Glaxo and also on rice diet. So to state that cow's milk alone is the cause of it is not borne out by facts. I think the real cause of the disease is the dyspepsia due to indiscriminate and untimely feeding and also overfeeding with any of the foods, cow's milk, artificial milk food or rice.

In this connection I have to state another fact. There are some proprietary Ayurvedic medicines for the successful treatment of the disease as Zammi's 'Liver Cure' and Tekkali medicines. They advise to avoid proprietary milk foods and give only cow's milk in the treatment of these diseases. Many cases are being cured by giving cow's milk and those Ayurvedic medicines. How then can we say that cow's milk is the cause of the disease?

2. About the treatment of the disease it is said in the article that three medicines can confidently be given, viz, streptomycin, choline and vitamin B complex. But the case reports given in the article are of early cases only with no jaundice and oedema or ascites. They are not yet tried on advanced cases with jaundice, oedema, etc. How then are we sure that the same three medicines are useful in the treatment of advanced cases also? Even cases with jaundice and oedema are being successfully treated with the above-mentioned Ayurvedic medicines. If cow's milk deficient in choline is the cause how can we explain the successful treatment of the cases with cow's milk alone and by the above Ayurvedic medicines?

Yours faithfully,
B. VASUDEVAMURTHY, L.M.P.

GUDIVADA,
KISTNA DIST.

[(1) Your correspondent writes that 'to state that cow's milk alone is the cause of it is not borne out by fact'.

In the first instance it is not correct to state that I have said 'cow's milk alone is the cause of it'. I wish to draw the attention of the correspondent to my article on infantile cirrhosis published in the *Pro. Acad. of Indian Sciences* (No. 3, Vol. XIV, Sec. B, 1941), wherein he will find a detailed discussion regarding cow's milk and the part it plays in bringing about this disease. Evidently the correspondent has not read my previous article nor the scientific views expressed by other workers in India and abroad in connection with my theory. I would rather say that his remark is not 'borne out by facts'.

(2) Your correspondent further writes as follows: 'I think the real cause of it is the dyspepsia due to indiscriminate and untimely feeding and overfeeding with any of the foods, either cow's milk or artificial milk foods or rice'. . . . 'Overfeeding', 'indiscriminate feeding', 'untimely feeding', etc., are all causes not only of cirrhosis but of any other diseases in children as well as adults; and these explanations come in very handy whenever a proper cause of a disease is not known or understood properly! Several contributors in India (excepting some scientific investigators) for the last 50 or 60 years have been repeating over and over again those words. I have discussed all aspects of 'errors of diet' in my first article at great length, after drawing attention to almost every publication on the subject. I have seen cirrhosis cases occurring in families both rich and poor; who have not committed any of those 'faults' mentioned above by your correspondent.

(3) Regarding the 'successful treatment by some proprietary powders, etc.' sold in the market as specifics, my reply would be as follows:

It is not within the scope of my article to discuss the efficiency or otherwise of any Ayurvedic drug and I do not propose to explain the 'how' or 'why' of those drugs or of these physicians. It is not correct to say that any drug or medicine put forth by any person other than an allopathic doctor is an 'Ayurvedic medicine'. All I wish to mention is that latest scientific investigations in the rest of the world have shown that 'there is an aetiological relationship either direct or indirect between nutritional deficiency and cirrhosis of the liver; and the malnourished liver

becomes more vulnerable to toxins'. In the light of these investigations and my own, certain lines of treatment were adopted by me and when the results were found to be good, they were published.

If your correspondent has found out any other drug to be useful, the best course open to him is to publish an article on the efficacy of the drug, giving out the composition, therapeutic action and method of administration, etc., instead of asking others to explain how the drug he has used acts.

(4) Regarding the effect of streptomycin in advanced cases of cirrhosis with ascites and jaundice, I have already stated in the article that I tried this drug on two such cases and both of them died. They are of no use in advanced cases (page 153). Probably this has escaped the notice of the correspondent.

Regarding the 'proprietary medicines' for curing infantile cirrhosis I wish to add the following few lines purely as a theoretical argument:—

(i) There are experimental and other scientific investigations and proofs to show that certain bacteria and toxins can produce cirrhotic changes in the liver which has become devitalized due to malnourishment, etc.; and that choline can prevent and cure cirrhosis.

(ii) If cirrhosis is cured or prevented by any of the 'proprietary medicines' according to your correspondent, then the natural conclusion would be (a) that these medicines contain directly or indirectly choline, or (b) the ingredients of that medicine are broken up or synthesized to form choline or a like substance which has the same effect as that of choline and (c) when such a medicine is used which supplies the deficiencies of milk there is no harm in giving milk simultaneously. If milk is not given to sick children what other substitute could they think of?

Your correspondent says that *they* (perhaps Ayurvedic physicians) advise to avoid proprietary milk foods. That is so for the reason that Ayurvedic physicians of ancient days could not have prescribed 'Glaxo' as it was not yet known to them and those of modern days do not prescribe it because it is 'non-Ayurvedic'.

I wish to say a few words regarding my experience with the so-called specific 'powders' and 'medicine' sold in the market. I desire, however, to make it clear that I do not wish to enter into any correspondence in future on the subject of these 'specific cures'. I have tried these medicines on several children and seen many more cases where these have been administered by parents and doctors for purposes of curing as well as for prophylaxis. A few of the important manufacturers of these medicines have come in person and discussed the subject with me. I have shown them my protocol containing the case records of those cases wherein I have used those drugs. Some of them were not 'qualified' medical men in any of the systems of medicine and yet they claimed to be capable of manufacturing 'Specifics' for liver cirrhosis. One of them was very candid and told me that he had earned enormous amount of money by selling his medicine although he was not an Ayurvedic physician, a 'qualified doctor' or well conversant with the signs and symptoms of the disease and differential diagnosis. He made an offer to supply his medicine free of cost to all my patients whenever a prescription came from me. I would have been the first person to advocate the use of those drugs, had I only found them to be useful.

I want to make yet another observation and it is this:

Considering the extensive propaganda for the sale of these 'specific cures' for cirrhosis by various methods of advertisements and considering the large quantity of these medicines used by parents and some doctors with the object of curing as well as preventing

this disease, year after year (as I know for the last 20 years), I am wondering why this disease has not vanished altogether yet, at least, in Mysore State, if not in other parts! These drugs are so easily available that parents themselves administer them to the children whether they have developed cirrhosis or not. Are not two decades sufficient for any 'efficient' and 'specific' drug when used so extensively to prevent and eradicate any disease? One need not wait for an answer.

P. KRISHNA RAO.]

PALUDRINE POISONING

SIR,—I may kindly be permitted to say a few words regarding paludrine (0.3 gm. doses). I feel myself that it is not quite right on my part to say anything about paludrine while I am working in the cinchona plantation.

Though malaria cases are very few here, still I get chances to prescribe paludrine to the people (suffering from malaria) coming from a long distance (*bustee* area), as they dislike to take quinine because of its bitter taste.

The patients have often complained of their bowel irregularities, pain in the abdomen and also headache which I have so far not considered important.

Now, finding the article in your journal of July 1950 under the heading 'A case of accidental paludrine poisoning' written by Dr. P. C. Sen, L.M.S., I find no cause to rule out the complaints regarding effects of paludrine which I had received previously.

Recently one patient under my observation who took 15 grains of quinine daily for 10 days for malaria, and at present taking 0.3 gm. tablet paludrine—one tablet twice a week (as prophylactic)—complains of acute gripping pain in the abdomen, indigestion, looseness of bowel practically amounting to diarrhoea and severe headache. These symptoms are evident all day and die down towards evening.

Though the drug has an advantage over quinine as a suppressive, can it be proper to persuade a patient to take the drug (paludrine) for an indefinite period—when the above complaint stands in the way?

Yours faithfully,
KAMAKHYA PROSAD DUTTA,
Medical Officer,
Government Cinchona Plantation,
Mungpoo.

MUNGPOO P. O.,
DIST. DARJEELING
(WEST BENGAL)

[In the vast majority of cases 'paludrine' in a dose of 0.3 gm. gives rise to no toxic manifestation whatsoever. A few cases have been reported, however, in which the administration of 0.3 gm. of paludrine has caused nausea, vomiting, epigastric discomfort and/or looseness of bowels. These untoward effects can be avoided generally if paludrine is given after food along with a glass of water. In any case it will not be advisable to persuade a patient to take the drug for an indefinite period if he cannot tolerate it. The case under reference, 'a case of accidental paludrine poisoning' reported in the July 1950 issue of this journal, is hardly comparable since the toxic symptoms in that patient were due to gross overdosage with paludrine.—R. N. C.]

KALA-AZAR IN INDIA AND THE SANDFLY

SIR,—I have just read in the August number of the *Indian Medical Gazette* (1950) Brook's condensation of the 'Case against the sandfly' and its rôle in the transmission of kala-azar and his further criticisms of the accepted theory. These criticisms are too valid and scathing to be ignored and it is wellnigh criminal to attempt to do so.

I wrote to your journal some time ago in this same trend but I observe that nothing has been done to banish, once and for all, from textbooks what the eminent medical scientist Dobell labels little more than 'a protozoological myth'.

Are we contributing to truth or toadying to the oracle who has spoken and dare not be contradicted?

Let the protagonists of the sandfly theory don their armour for the last time and come out into the daylight, to return their opponents' fire, if they can, but in doing so we must have facts by way of rebuttal—not merely sarcasm or irony.

Is not the newly re-organized Indian Council of Medical Research the correct body to look to for final proof? I think it is their bounden duty to take this matter up and award the honours where they are due. What will the next generation of enquirers think of us if this matter is allowed to drop? I feel sure there is someone strong enough to explode a textbook untruth in the interest of Truth itself.

One point more, Sir, why has the reviewer in the *Tropical Diseases Bulletin* not yet said anything about Malone's Rejoinder (1947) and Brook's letter in the *Indian Medical Gazette* (1949)? Does he not consider these worthy of his notice or is it 'suppressio veri'?

Science and Truth are inseparable and neither bows to person, position or prestige; so, in spite of damage to reputations of those in high authority, let us have the Truth now. Six years is long enough to have waited for it.

Yours faithfully,
B. J. BOUCHÉ, M.R.C.S., L.R.C.P.,
MAJOR, I.M.D. (Retd.).

INVERNEAL LODGE,
MUSSOORIE, U. P.,
21st September, 1950.

REFERENCES

- MALONE, R. H. (1947) .. *Indian Med. Gaz.*, **82**, 544.
BROOKS, A. G. (1949) .. *Ibid.*, **84**, 224.
Idem (1950) .. *Ibid.*, **85**, 380.

SULPHA AND SULPHONE DRUGS

SIR,—Your May issue is just in our hand and we have gone through an article as published in page 202 under the caption: 'Chemotherapy of cholera with a new sulphone compound'. The compound used is formo-cibazol which is a sulfathiazole derivative. No sulphone compound has been used in the trial. How then in the caption the expression, New Sulphone, appeared.

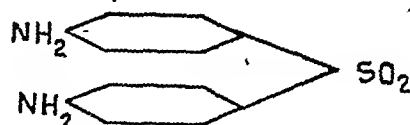
Yours faithfully,
U. P. BASU, D.Sc., F.N.I.,
Director.

BENGAL IMMUNITY
RESEARCH INSTITUTE,
CALCUTTA.

[Regarding the sulpha and sulphone drugs, the parent compound is



and all sulpha drugs are its derivatives, while the drugs commonly known as sulphones are derivatives of diamino-diphenyl sulphone.



For the sake of clarity it is better to alter it to 'Sulpha' instead of 'Sulphone Drugs'.—M. ABDULLA.]

[In this connection also see editorial on 'Sulphonamides and sulphones' in this issue.—EDITOR, I.M.G.]

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

INDEX TO VOL. LXXXV

OF

"THE INDIAN MEDICAL GAZETTE"

For the year 1950

[Original Article 'O. A.'; Mirror of Hospital Practice 'M. H. P.'; Editorial 'E.'; Special Article 'S. A.'; Medical News 'M. N.'; Public Health Section 'P. H. S.'; Current Topics 'C. T.'; Correspondence 'C.'; Therapeutic Notes 'T. N.'; Any Questions 'A. Q.'; *Italics* signify Reviews; Reviews are placed under the name of the author; they also appear under the heading 'Reviews'; where they are arranged according to subjects.]

	Page		Page		Page
A		Ambulance Planc, New Design (M. N.) ..	114	Anderson, H. H., <i>et al.</i> Thioarsenites in Amœbiasis (C. T.) ..	221
Abdominal Disease, Acute (Cope) (C. T.) ..	573	Amœbiasis, Aureomycin Treatment of (C. T.) ..	276	————— <i>W. A. D. Edited by Pathology</i> ..	331
————— Surgery, Last Twenty Years of (Kinnear) (C. T.) ..	577	————— Cutaneous (Ghosh and Mukherji) (O. A.) ..	339	Aneurysmal Bone Cyst (Bhende and Kothare) (O. A.) ..	544
Abdulla, M., and Rohini, D. K. Chemotherapy of Cholera with a New Sulphone Compound (O. A.) ..	202	————— Cutaneous, A Case of (Armstrong) (C. T.) ..	475	Angina Pectoris after Virus Disease, Unusual Cure of (Thakkar) (C.) ..	84
Abreast with the Times (E.) ..	307	————— Hepatic, Chloroquine and (C. T.) ..	125	Aniline Marking on Diapers, Poisoning from (C. T.) ..	125
Abscess, Breast (Chacko) (M. H. P.) ..	157	————— Hepatic, with Chloroquine, Treatment of (Conan) (C. T.) ..	221	Antacids, New—Aluminum Glutamates (C. T.) ..	329
Accident Prevention in Factories (Coller) (M. N.) ..	72	————— in Infancy (De Silva) (C. T.) ..	274	Anti-Arthritic Drug, Search for New Source of (Williams) (M. N.) ..	411
Acne in General Practice, The Management of (Jolly and Kopfler) (C. T.) ..	425	————— Thioarsenites in (Anderson <i>et al.</i>) (C. T.) ..	221	Antibiotic Therapy, Continuous (Steimberg) (C. T.) ..	478
ACTH, Cortisone and, in Man, Observations on the Physiologic Effects of (Sprague <i>et al.</i>) (C. T.) ..	522	————— Thioarsenites in (C. T.) ..	373	Antibiotics in Primary Atypical Pneumonia (C. T.) ..	124
Advertisements in Medical Journals (Mukherjee) (C.) ..	434	————— Thoracic (Bookless) (C. T.) ..	526	Antihistamine Drug, A Case of Acute Nephritis Treated with an (Samad and Kapoor) (M. H. P.) ..	208
Afghanistan Monarch Visits W.H.O. (M. N.) ..	111	————— Thoracic Complications of (C. T.) ..	280	Antihistamines, A Colorimetric Assay for (C. T.) ..	329
Ahuja, M. L., and Brooks, A. G. Heparin in Yellow Fever (C.) ..	233	Amœbic Abscess of the Brain (Koshy) (O. A.) ..	287	Anti-Histaminic Drug, Two Cases of Vesicular (Weeping) Eczema Treated with (Sen) (M. H. P.) ..	54
————— M. L., and Brooks, A. G. Hydrophobia in India (O. A.) ..	449	————— Abscess of the Liver, Refractory, Treated with Chloroquine (Emmett) (C. T.) ..	182	Anti-Malaria Project (W.H.O.) in Remote Area of Afghanistan (M. N.) ..	460
Aid in Relief Programmes for Civilians, W.H.O. to Send Health Officers to Korea to (M. N.) ..	463	————— Abscess, Multiple, of the Lungs (Chatterjee and other) (C. T.) ..	281	Antimalarials, Studies in (Roy <i>et al.</i>) (M. N.) ..	512
Air-Cooled Buildings and Electric Fans (C. T.) ..	423	————— Dysentery and Liver Disease (Chakravarti) (O. A.) ..	394	Antiserum, A Death from (C. T.) ..	580
Air Pollution, Modern Crumbling Ancient Monuments of Greece (C. T.) ..	525	————— Liver Abscess, Chloroquine in the Treatment of (Harinasuta) (O. A.) ..	37	Antitetanus Inoculation (M. N.) ..	108
Allen, F. H., <i>et al.</i> Erythroblastosis Fœtalis (C. T.) ..	376	Amyloidosis, Primary Systemic (Wahi and Tandon) (O. A.) ..	537	Anti-Thyroidin, Fibrolysin and, on Raynaud's Disease, Effect of (Datta and Thakurta) (M. H. P.) ..	102
Allison, D. R. Pain in the Chest Wall Simulating Heart Disease (C. T.) ..	527	Anæmia, Nutritional Megaloblastic: So-called Pernicious Anæmia of Pregnancy (Kothari and other) (C. T.) ..	422	Anuria, Management of (Miller) (C. T.) ..	377
Aluminium Monostearate, Procaine Penicillin with, The Use in Children of (Emery <i>et al.</i>) (C. T.) ..	123	————— Pernicious, Folic Acid and Neurologic Changes in (C. T.) ..	181	Appeal, An (Mehta) (C.) ..	233
Aluminum Glutamates—New Antacids (C. T.) ..	329	————— of Pregnancy, Pernicious (Furman <i>et al.</i>) (C. T.) ..	576	Argemone and Mustard Seeds (Sanyal) (O. A.) ..	498
————— Hydroxide, Aureomycin and (Waisbren and other) (C. T.) ..	276			Armstrong, W. A Case of Cutaneous Amœbiasis (C. T.) ..	475
				Arsenoxide Derivatives, Studies on, Part I (Bose <i>et al.</i>) (O. A.) ..	50
				Artane Therapy for Parkinsonism (Doshiay and other) (C. T.) ..	276

	Page		Page		Page
Arthroplasty, Cup, in Hip-Joint Surgery (Kini and Naidu) (O. A.) ..	19	Auscultatory Method for Ascertaining the Size of the Liver (Rinzler) (C. T.) ..	577	Berberian, D. A., and other. The Effect of Chloroquine Diphosphate on Malaria Splenomegaly (C. T.) ..	128
Arthritis, Gonococcal (Malhotra) (O. A.) ..	187	Respiratory Murmur (C. T.) ..	330	Bernard Shaw Passes On (E.) ..	505
Remissions in (C. T.) ..	273			Berry, J. N. Congenital Atonic Diplegia (O. A.) ..	195
Rheumatoid, in a Child with Unusual Manifestations (Mukherjee) (O. A.) ..	247	B		J. N. Metaphysial Aclasis (O. A.) ..	387
Rheumatoid, Deoxycortone Acetate and Ascorbic Acid in the Treatment of (Vay and other) (C. T.) ..	274	BAL and Uranium Poisoning (C. T.) ..	280	Betel Leaf, Antibacterial Principle of the (Pai and other) (O. A.) ..	302
in Smallpox, Incidence of (Chatterjee) (O. A.) ..	49	B.C.G. Vaccination, Protective Value of (P. H. S.) ..	74	Bettley, F. R. Skin Diseases in General Practice ..	32
Ascaris Lumbricoides, An Observation on Preserved Ova of (Sen Gupta and Mitra) (O. A.) ..	138	Babies, Sudden Death of (Ray) (C.) ..	133	Bevan to Visit India (M. N.) ..	364
Ascites, The Effect of Rigid Sodium Restriction in Patients with Cirrhosis of the Liver and (Eisenmenger <i>et al.</i>) (C. T.) ..	475	Suffocation, often Wrong Diagnosis (M. N.) ..	173	Bhadury, K. P. A Case of Submucous Fibroid Simulating Pregnancy (M. H. P.) ..	345
Ascorbic Acid, Deoxycortone Acetate and, in the Treatment of Rheumatoid Arthritis (Vay and other) (C. T.) ..	274	Back-Room-Boys of Medicine Get New Headquarters (M. N.) ..	312	K. P. Epidemic Dropsy Complicating Pregnancy (O. A.) ..	98
Acid, Vitamin B ₁₂ and, An Incompatibility Between (C. T.) ..	329	Bacteriophage, Treatment of Typhoid Fever with (Biswas) (C.) ..	583	Bhalehndra Krishna Memorial Gold Medal of the Bombay Medical Union (M. N.) ..	29
Asher, R. Myxoedematous Madness (C. T.) ..	222	Treatment of Typhoid Fever with (Dhayagude and other) (C. T.) ..	423	Bhaskaran, T. R., <i>see</i> Subrahmanyam, K. The Risk of Pollution of Ground Water from Borehole Latrines (P. H. S.) ..	418
Asthma, Bronchial, Isopropyl-epinephrine and (C. T.) ..	126	Bajpayee, A. P. Uttar Pradesh Medical Council (M. N.) ..	362	Bhatt, S. S. Physical Therapy Journals (A. Q.) ..	334
Temporary Relief of, by Jaundice (Gorin) (C. T.) ..	130	Banerjee, A. C. Minutes of the Meeting of the United Provinces Medical Council, Lucknow (M. N.) ..	113	Bhattacharjee, S. K. An Unusual Case of Elephantiasis Buttocks (M. H. P.) ..	158
Atom Bomb Made Easy (E.) ..	405	R. K. The Use of Potassium Permanganate in the Disinfection of Water (P. H. S.) ..	214	Bhattacharya, B., <i>see</i> Sen Gupta, P. C., and Basu Mallick, K. C. A Rapid Method of Iron Haematoxylin Stain for Protozoa in Tissue Sections and Smears (O. A.) ..	400
Aureomycin and Aluminum Hydroxide (Waisbren and other) (C. T.) ..	276	Banerjee, A. K., <i>see</i> Panja, D. Perionychia due to Monilia Infection (O. A.) ..	137	Bhende, Y. M., and Kothare, S. N. Aneurysmal Bone Cyst (O. A.) ..	544
by Aluminum Hydroxide Gel, Adsorption of (C. T.) ..	329	A. K., <i>see</i> Panja, D., and Gupta, J. C. Aureomycin, in the Treatment of Pemphigus Foliaceus (M. H. P.) ..	503	Y. M., Purandare, N. M., Banker, D. D., Figueredo, N., and Desai, S. D. Outbreak of Kala-Azar in an Institution in Bombay (O. A.) ..	237
in Brucellosis (C. T.) ..	221	A. K., <i>see</i> Sen Gupta, P. C., and Panja, D. An Unusual Case of Post-Kala-Azar Dermal Leishmaniasis (O. A.) ..	138	Bhowmick, S. K. A Case of Myiasis of the Nasal Cavity (M. H. P.) ..	306
The Clinical Evaluation of (Brainerd <i>et al.</i>) (C. T.) ..	428	D., <i>see</i> Konar, N. R. Disseminated Lupus Erythematosus (O. A.) ..	188	Biliary Tract Infection, Streptomycin in (Chaudhuri and Chakravarti) (M. H. P.) ..	555
in Infections of the Urinary Tract (Franklin) (C. T.) ..	179	Banerji, B. Advent of Elkosin (O. A.) ..	298	Binder, M. L., and other. Treatment of Herpes Zoster with Aureomycin (C. T.) ..	277
in Kala-Azar (Gupta and Sen Gupta) (C.) ..	384	Bang, H. O., <i>et al.</i> Low-Salt Diet in Treatment of Hypertension and Hypertensive Heart Disease (C. T.) ..	273	Biological Warfare, Control of (C. T.) ..	424
Pertussis and (Beel <i>et al.</i>) (C. T.) ..	220	Banker, D. D., <i>see</i> Bhende, Y. M., Purandare, N. M., Figueredo, N., and Desai, S. D. Outbreak of Kala-Azar in an Institution in Bombay (O. A.) ..	237	Biometric Studies of School Children of Hyderabad State (Daver) (P. H. S.) ..	412
found to be Potent Growth Factor as well as Drug (C. T.) ..	523	Barbiturate Poisoning Treated with Picrotoxin (Konar and Das) (O. A.) ..	494	Birnberg, C. H. Female Sex Endocrinology ..	228
Therapy in Human Brucellosis due to <i>Brucella abortus</i> (Braude <i>et al.</i>) (C. T.) ..	277	Bardhan, P. N., <i>see</i> Dutt, M. Experience with Floccillin '96' (O. A.) ..	199	Biswas, N. Treatment of Typhoid Fever with Bacteriophage (C.) ..	583
Treatment of Amebiasis (C. T.) ..	276	Basu, U. P. Sulpha and Sulphone Drugs (C.) ..	534	Blanc, G. Plague (M. N.) ..	69
in the Treatment of Gonorrhoea, Oral Administration of (Chen <i>et al.</i>) (C. T.) ..	127	Basu Mallick, K. C., <i>see</i> Sen Gupta, P. C., and Bhattacharya, B. A Rapid Method of Iron Haematoxylin Stain for Protozoa in Tissue Sections and Smears (O. A.) ..	400	G. Plague (C. T.) ..	129
Treatment of Herpes Zoster with (Binder and other) (C. T.) ..	277	Beaumont, G. E. Applied Medicine ..	430	Blind Physician, New Appointment for (M. N.) ..	510
in the Treatment of Infectious Diseases (Rose and other) (C. T.) ..	476	Beaver, P. C. Methods of Pinworm Diagnosis (C. T.) ..	128	Blocker, T. G., and other. Surgical Treatment of Elephantiasis of the Lower Extremities (C. T.) ..	428
in the Treatment of Pemphigus Foliaceus (Panja <i>et al.</i>) (M. H. P.) ..	503	Beirwaltes, W. H., and other. The Present Status of the Treatment of Thyrotoxicosis (C. T.) ..	127	Blood Cell Counts and Haemoglobin Determination (C. T.) ..	374
in the Treatment of Typhoid, Typhus, Cystitis and Pertussis (Krishnan <i>et al.</i>) (O. A.) ..	202	Bentley, C. A. (M. N.) ..	172	Donation Service, Australia's (Kelly) (M. N.) ..	465
				Normal, Some Constituents in (Gokhale and Lokre) (O. A.) ..	94
				Body Fluids, Various, The Cytological Diagnosis of Malignant Cells in (Taylor and other) (C. T.) ..	182
				Body-Weight to the Weights of the Organs, The Relationship of (Gharpure and Jhala) (O. A.) ..	342
				Bookless, A. S. Thoracic Amebiasis (C. T.) ..	526

Page		Page		Page	
Borehole Latrines, The Risk of Pollution of Ground Water from (Subrahmanyam and Bhaskaran) (P. H. S.) ..	418	Cataract Extraction, Separation of Lids by Lid Sutures in (Dhir) (O. A.) ..	149	Chaudhuri, R. N., and Chakravarti, H. Streptomycin in Biliary Tract Infec- tion (M. H. P.) ..	555
Bose, A., <i>see</i> Lal, S. B. Use of Defatted Groundnut Cake Flour as Food (P. H. S.) ..	322	Cattle Fodder, Groundnut Husk as (M. N.) ..	363	— R. N., <i>see</i> Chakra- varti, R. N., and Chakravarty, N. K. Epidemic Dropsy: A New Test for Arge- mone Oil (O. A.) ..	344
— A. N., Bose, S., and Ghosh, T. N. Studies on Arse- noid Derivatives, Part I (O. A.) ..	50	Chacko, A. G. Abscess Breast (M. H. P.) ..	157	— R. N., and Chakra- varti, N. K. Treat- ment of Epidemic Dropsy (S. A.) ..	165
— J. P. Insulin Resistance in Diabetes Patients (O. A.) ..	445	Chakravarti, H. Studies on Plasma Protein. I. Kala-Azar (O. A.) ..	141	— R. N., Ghosal, S., and Rai Chaudhuri, M. N. Chloromycetin in the Treatment of Cholera (O. A.) ..	398
— S., <i>see</i> Bose, A. N., and Ghosh, T. N. Studies on Arsenoid Derivatives, Part I (O. A.) ..	50	— H. Studies on Plasma Protein. II. Amoebic Dy- sentery and Liver Disease (O. A.) ..	394	— R. N., <i>see</i> Krishnan, K. V., Chakravarti, H., and Rai Chau- dhuri, M. N. Aureo- mycin in the Treat- ment of Typhoid, Typhus, Cystitis and Pertussis (O. A.) ..	202
Bouche, B. J. Kala-Azar in India and the Sandfly (C.) ..	534	— H. Malaria (O. A.) ..	500	Chemistry and Physics, Post- Doctorate Fellowships in (M. N.) ..	562
Bourne, A. W. A Synopsis of Obstetrics and Gynaecology ..	32	— H., <i>see</i> Chaudhuri, R. N. Streptomycin in Biliary Tract Infection (M. H. P.) ..	555	Chen, C. H., <i>et al.</i> Oral Ad- ministration of Aureomycin in the Treatment of Gonorrhœa (C. T.) ..	127
Bower, A. G., <i>et al.</i> Use of Curare in the Treatment of Anterior Poliomyelitis (C. T.) ..	580	— H., <i>see</i> Krishnan, K. V., Chaudhuri, R. N., and Rai Chaudhuri, M. N. Aureomycin in the Treatment of Ty- phoid, Typhus, Cys- titis and Pertussis (O. A.) ..	202	Chest Radiographic Unit, Mass (M. N.) ..	560
Brainerd, H., <i>et al.</i> The Clinical Evaluation of Aureomycin (C. T.) ..	428	— R. N., Chaudhuri, R. N., and Chakra- varty, N. K. Epi- demic Dropsy: A New Test for Argemone Oil (O. A.) ..	344	Child Welfare Work, Maternity and, in Railway Colonies (Chopra) (P. H. S.) ..	317
Brammall, C. C. D. Menace of the 'Dusted' Lung (M. N.) ..	265	— R. N., and Sen Gupta, P. C. Uri- nary Excretion of Antimony after Administration of Methyl Glucamine Antimoniate (O. A.) ..	388	Children's Doctors and Nurses Planned, Delhi Training Centre for (M. N.) ..	461
Braude, A. I., <i>et al.</i> Aureomycin Therapy in Human Brucellosis due to <i>Brucella abortus</i> (C. T.) ..	277	Chakravarty, N. K., <i>see</i> Chakra- varti, R. N., and Chaudhuri, R. N. Epidemic Dropsy: A New Test for Argemone Oil (O. A.) ..	344	Chloramphenicol (Chloromycetin), Clinical Use of the Antibiotic (Smadel) (C. T.) ..	523
Breast, Human, Squamous Meta- plasia and Keratinization in Cystic Hyperplasia of the (Rangam) (O. A.) ..	9	— N. K., <i>see</i> Chau- dhuri, R. N. Treat- ment of Epidemic Dropsy (S. A.) ..	165	— Pertussis Treated with (Payne <i>et al.</i>) (C. T.) ..	424
Briggs, J. N. Relapse in Typhoid Fever after Treatment with Chloramphenicol (C. T.) ..	475	Chanda, N. K., <i>see</i> Tribedi, B. P. Post-Neerotic Scarring of the Liver in a Child and Its Pos- sible Relationship to Rh Factor (O. A.) ..	192	— Relapse in Ty- phoid Fever after Treatment with (Briggs) (C. T.) ..	475
British Journal of Tuberculosis and Diseases of the Chest (M. N.) ..	467	Chandra, N. K., and other. Cooley's Anemia (C. T.) ..	527	— Therapy, Re- lapses in Typhoid to Duration of (C. T.) ..	370
— Medical Association, Annual Meeting of the ..	177	Chatterjee, P. K., and other. Multiple Amoebic Abscess of the Lungs (C. T.) ..	281	— Therapy, Rela- tion of Relapses in Typhoid to Duration of (Smadel <i>et al.</i>) (C. T.) ..	220
— Surgeons Invited to Yugoslavia (M. N.) ..	264	— R. N. Incidence of Arthritis in Smallpox (O. A.) ..	49	— in Treatment of Infantile Gastro- Enteritis (Rogers <i>et al.</i>) (C. T.) ..	272
Brooks, A. G., <i>see</i> Ahuja, M. L. Heparin in Yellow Fever (C.) ..	233	— S. Penicillin and Sulphadiazine in Lobar Pneumonia (C.) ..	233	— in Typhoid Fever (Shah) (C. T.) ..	526
— A. G., <i>see</i> Ahuja, M. L. Hydrophobia in India (O. A.) ..	449	Chaudhuri, R. N. Notes on Some Remedies. XXXII. Dehydration and Its Treatment, Part IV. (T. N.) ..	57	Chlorguanide Hydrochloride and Malaria (C. T.) ..	526
— A. G. Clinical Hydro- phobia without Contact with Rabies Transmitting Animal (C.) ..	133	— R. N. Notes on Some Remedies. XXXIII. Dehydration and Its Treatment, Part IV. Dehydration in Infants (contd.) (T. N.) ..	105	Chloromycetin in Scrub-Typhus (Giles and other) (C. T.) ..	274
— A. G. Kala-Azar in India and the Sandfly (C.) ..	380	— R. N. Notes on Some Remedies. XXXIV. Dehydration and Its Treatment, Part V. Treatment of Cholera (T. N.) ..	257	— in the Treatment of Cholera (Chau- dhuri <i>et al.</i>) (O. A.) ..	398
Brown, R. C., and Dobbs, R. H. Midwifery ..	581			— in Typhoid and Paratyphoid Fever (Treu) (O. A.) ..	154
Brucellosis, Aureomycin in (C. T.) ..	221			Chloroquine Diphosphate on Malaria Spleno- megaly, The Effect of (Berberian and other) (C. T.) ..	128
— Human, due to <i>Brucella abortus</i> , Aureomycin Therapy in (Braude <i>et al.</i>) (C. T.) ..	277			— and Hepatic Amœ- biasis (C. T.) ..	125
Burrows, W. Textbook of Bac- teriology ..	332				
C					
Campbell, K. N., <i>et al.</i> Follow- up Study of Patient with Thromboangiitis Obliterans (C. T.) ..	520				
Cancer of the Breast (C. T.) ..	279				
— Hospital in Calcutta (M. N.) ..	316				
— Treatment, New Super X-Ray Machines for (M. N.) ..	460				
Cancer-causing Chemical Can now be Traced through the Body (C. T.) ..	525				
Carroll, G., <i>et al.</i> Gantrisin in the Treatment of Urinary Infections (C. T.) ..	526				

Page		Page		Page
Chloroquine, Intramuscular, The Treatment of Falciparum Malaria with (Spicknall <i>et al.</i>) (C. T.) .. 476		Cortisone and ACTH in Man, Observations on the Physiologic Effects of (Sprague <i>et al.</i>) (C. T.) .. 522	Deaf May 'Hear Through Their Fingers' (M. N.) .. 109	
Refractory Amœbic Abscess of the Liver Treated with (Emmett) (C. T.) .. 182		in the Treatment of Rheumatism (C. T.) .. 124	Death Rate in the United States (M. N.) .. 109	
in the Treatment of Amœbic Liver Abscess (Harinasuta) (O. A.) .. 37		Coupon System, Unesco (M. N.) .. 312	Deformities, Congenital, Theories of the Etiology of (Kiskadden <i>et al.</i>) (C. T.) .. 223	
Treatment of Hepatic Amœbiasis with (Conan) (C. T.) .. 221		Crews, W., and other. A Case of Severe Generalized Reaction to Mosquito Bites (C. T.) .. 377	Dehydration in Infants (Chaudhuri) (T. N.) .. 57	
Cholera, Chloromycetin in the Treatment of (Chaudhuri <i>et al.</i>) (O. A.) .. 398		Cross, W. G. Oral Reactions to Penicillin (C. T.) .. 31	in Infants (contd.) (Chaudhuri) (T. N.) .. 105	
in Hyderabad State (Melita) (P. H. S.) .. 569		Curds, Indian or 'Dahi' as a Source of Vitamin B Complex (Joshi) (C. T.) .. 376	and its Treatment, Part V. Treatment of Cholera (Chaudhuri) (T. N.) .. 257	
Koch and (M. N.) .. 512		Currie, J. R., and other. Hygiene .. 228	Dental Congress, Eleventh International (M. N.) .. 308	
with a New Sulphone Compound, Chemotherapy of (Abdulla and Rohini) (O. A.) .. 202		Curry, J. J., and other. Continuous Intravenous Injection of Typhoid Vaccine in Treatment of Certain Ophthalmic Diseases (C. T.) .. 121	Congress, XIth International (M. N.) .. 560	
and the Rationale of Treatment, Clinical and Biochemical Studies in (Ghanen and other) (C. T.) .. 478		J. J., and other. Continuous Intravenous Injection of Typhoid Vaccine in Treatment of Certain Ophthalmic Diseases (C. T.) .. 224	Dentists, Registration of (M. N.) .. 174	
Treatment of (Chaudhuri) (T. N.) .. 257		Cutaneous Diseases, Roentgen Rays in the Treatment of (Lane) (C. T.) .. 580	Deoxycortone Acetate and Ascorbic Acid in the Treatment of Rheumatoid Arthritis (Vay and other) (C. T.) .. 274	
Treatment of (Gupta) (C.) .. 584		Cutler, J. C. The Venereal Disease Programme of the World Health Organization (O. N.) .. 22	Dermal Leishmaniasis, Post Kala-Azar, An Unusual Case of (Sen Gupta <i>et al.</i>) (O. A.) .. 138	
Chopra, B. L. Maternity and Child Welfare Work in Railway Colonies (P. H. S.) .. 317		Cysticercosis Cellulosa, Generalized (Dave) (O. A.) .. 92	Dermatology, Tenth International Congress of (Mitchell-Heggs) (M. N.) .. 558	
R. N., <i>et al.</i> A Treatise on Tropical Therapeutics (Kagan and other) (C. T.) .. 225		Cellulosa, Generalized (Dave) (C.) .. 433	Desai, S. D., <i>see</i> Bhende, Y. M., Purandare, N. M., Banker, D. D., and Figueredo, N. Outbreak of Kala-Azar in an Institution in Bombay (O. A.) .. 237	
Christopher, F. Edited by—A Textbook of Surgery by American Authors .. 131		Cystitis, Pertussis, Typhoid, Typhus, Aureomycin in the Treatment of (Krishnan <i>et al.</i>) (O. A.) .. 202	Deshmukh, P. L. Clinical Hydrophobia without Contact with Rabies Transmitting Animal (C.) .. 483	
Cirrhosis of the Liver and Ascites, Effect of Rigid Sodium Restriction in Patients with (Eisenmenger <i>et al.</i>) (C. T.) .. 475		Czechoslovakia withdrawn from W.H.O. (M. N.) .. 267	and 'Myotatic Irritability' (O. A.) .. 197	
of the Liver, Infantile, Treatment of (Rao) (O. A.) .. 150			P. L. A Note on Filing Medical Journals (C.) .. 284	
Clark-Kennedy, A. E. Lectures on Medicine to Nurses .. 379			Dey, A. C. Combination of Liver Extract and Folic Acid (C.) .. 34	
Clinical Meeting, First, of the Calcutta School of Tropical Medicine (M. N.) .. 563			N. C., <i>see</i> Ghosh, L. M., and Panja, D. Madura Foot (Mycetoma) (O. A.) .. 288	
Coggeshall, L. T., and other. Cure of Chronic Vivax Malaria with Pentaquine (C. T.) .. 122			Dharmendra. The Present Status of Sulphones in the Treatment of Leprosy (S. A.) .. 348	
Cohn, H. F., <i>et al.</i> Current Therapy .. 431			The Present Status of Sulphones in the Treatment of Leprosy (Erratum) .. 456	
Coller, S. G. Accident-Prevention in Factories. How Britain Safeguards Workers' Health (M. N.) .. 72			ie, R. G., and other. Out of Typhoid Fever Bacteriophage (C. T.) .. 423	
Colonna, P. C., and other. The Disc Syndrome (C. T.) .. 122			K. Separation of Lids Sutures in Cataract (O. A.) .. 149	
Conan, N. J. Treatment of Hepatic Amœbiasis with Chloroquine (C. T.) .. 221			Insulin Resistance (O. A.) .. 100	
Contact Lenses, Toleration of (C. T.) .. 280			Studies of the Action of Nicotinic Acid and Rao) .. 100	
Convulsive Therapy, Intensified Electrical, in a Military Hospital (Singh) (O. A.) .. 41			Sulphone by of Leprosy (T.) .. 100	
Cook, W. A. The Nerve Supply to the Maxillary Incisors (C. T.) .. 521			Centr .. 100	
Cooley's Anæmia (Chandra and other) (C. T.) .. 527				
Cooray, G. H., and Joseph, P. A. P. A Case of Xeroderma Pigmentosa in a Sinhalese (M. H. P.) .. 101				
Cope, V. Z. Acute Abdominal Disease (C. T.) .. 573				

	Page		Page		Page
Diplegia, Congenital Atonic (Berry) (O. A.) ..	195	Index for Volume 84, 1949 (E.) ..	66	Evans, C. L. Principles of Human Physiology (Starling) ..	33
Directors of Public Health Meet in Kandy (M. N.) ..	508	Para-aminosalicylic Acid : PAS ..	107	Ewing's Tumour (McSwain et al.) (C. T.) ..	122
Disc Syndrome (Colonna and others) (C. T.) ..	122	Polio Yet Again ..	108	Eye Operations, Televising (M. N.) ..	411
Dobell, Clifford (M. N.) ..	313	The Hormones ..	159		
Doggart, J. H. Ophthalmic Medicine ..	132	Geriatric Medicine ..	209		
Domus Chirurgico (M. N.) ..	365	Against Pessumism in Tuberculosis ..	261		
Doshay, L. J., and other. Artauc Therapy for Parkinsonism (C. T.) ..	276	Abreast with the Times ..	307		
Doyle, L. Handbook of Obstetrics and Diagnostic Gynaecology ..	430	Leprosy Tamed ..	347		
Drug Addiction, W.H.O. Experts on, Meet to Advise U.N. (M. N.) ..	72	Atomi Bomb Made Easy ..	405		
Drugs Act, 1940 (Saksena) (M. N.) ..	270	Rabies ..	457		
—Act, 1940 (M. N.) ..	511	George Bernard Shaw Passes On ..	505	F	
—Rules, 1945 (Saksena) (M. N.) ..	70	Sulphonamides and Sulphones ..	506	F. L. S. The Homœopathic Medical School ..	326
—Rules, 1945 (Saksena) (M. N.) ..	113	The Treponematoses ..	506	Faculty of Tropical Medicine and Hygiene, Bengal, D.T.M. Results, 1949-50 (M. N.) ..	177
—Rules, 1945 (Saksena) (M. N.) ..	270	Sudden Heart Failure ..	557	Famine Mortality, Lord Curzon on the ..	572
—Rules, 1945 (Saksena) (M. N.) ..	365	Polio: Two New Points ..	558	Farrer-Brown, L. Nuffield Foundation Travelling Fellowships Awards to Indian Graduates (M. N.) ..	468
—Rules, 1945 (Saksena) (M. N.) ..	511	Dr. K. S. Ray Educational Tour of Great Britain (M. N.) ..	559	Farris, E. J., and other. Edited by—The Rat in Laboratory Investigation ..	283
—Rules, 1945, Amendment (Saksena) (M. N.) ..	406	Eisenmenger, W. J., et al. The Effect of Rigid Sodium Restriction in Patients with Cirrhosis of the Liver and Ascites (C. T.) ..	475	Fibroid, Submucous, Simulating Pregnancy (Bhadury) (M. H. P.) ..	345
—Rules, 1945, Amendments to (Saksena) (M. N.) ..	28	Elephantiasis Buttocks, An Unusual Case of (Bhattacharjee) (M. H. P.) ..	158	Fibrolysin and Anti-thyroidin on Raynaud's Disease, Effect of (Datta and Thakurta) (M. H. P.) ..	102
—and Surgical Instruments, Meeting, Medical Profession's Need of (M. N.) ..	71	—of the Lower Extremities, Surgical Treatment of (Bloeker and other) (C. T.) ..	428		
Duck Eggs, Hospital Outbreak of Enteritis due to (Garrod and other) (C. T.) ..	278	Elkosin, Advent of (Banerji) (O. A.) ..	298	Fifty Years Ago.	
Duke-Elder, S. The Practice of Refraction ..	132	Emery, J. L., et al. The Use in Children of Procaine Penicillin with Aluminum Monostearate (C. T.) ..	123	The Calcutta Health Officer's Report ..	29
—W. S. Textbook of Ophthalmology, Vol. IV ..	182	Emmett, J. Refractory Amoebic Abscess of the Liver Treated with Chloroquine (C. T.) ..	182	Organizations for Research ..	77
Dunbar, F., et al. Synopsis of Psychosomatic Diagnosis and Treatment ..	81	Empyema following Closed Intrapleural Pneumolysis (Dingley) (O. A.) ..	337	Recent Italian Work on Mosquito Malaria ..	119
Dunkerley, G. E. Intravenous Saline (O. A.) ..	3	Endamaba histolytica Cultures, Synergistic Action of Penicillin and Streptomycin on (Seneca et al.) (C. T.) ..	125	The Annual Meeting of the British Medical Association ..	177
Dutch Archives of Surgery, The (M. N.) ..	117	Endocarditis, Healed Subacute Bacterial (Kaplan et al.) (C. T.) ..	182	The Teaching of Hygiene in Indian Universities ..	219
Dutt, M., and Bardhan, P. N. Experience with Floccillin '96' (O. A.) ..	199	Entamaba histolytica, The Food Habits of (Hoare) (C. T.) ..	474	Tuberculosis in India ..	271
Dutta, K. N. Medical Correspondence College (C.) ..	34	Enteritis due to Duck Eggs, Hospital Outbreak of (Garrod and other) (C. T.) ..	278	The Homœopathic Medical School ..	326
—K. P. Paludrine Poisoning (C.) ..	533	Eosinophilia, Epidemic of Cave-Borne Pulmonary Infiltrations with (C. T.) ..	330	Filarial Metamorphosis in the Anopheles ..	326
Dutta Gupta, A. K., see Tribedi, B. P. Tumours of Endothelial Origin (O. A.) ..	239	—Tropical, Studies on the Effect of the Administration of Pituitary Adrenocorticotrophic Hormone to a Case of Loeffler's Syndrome and (Herbert et al.) (C. T.) ..	474	A Garbled Quotation ..	326
Dysentery, Acute Bacillary, Comparative Value of Sulphadiazine and Sulphaguanidine in the Treatment of (Khan) (O. A.) ..	490	Epidemic Dropsy (Chakravarti et al.) (O. A.) ..	344	The Value of 'Sags' as Antiscorbutics in the Jail Dietary ..	327
		—Dropsy, Complicating Pregnancy (Bhadury) (O. A.) ..	98	Our Special Number ..	368
		—Dropsy, Treatment of (Chaudhuri and Chakravarty) (S. A.) ..	165	London Letter ..	421
		Epilepsy as a Sequela of Recurrent Malaria (Talbot et al.) (C. T.) ..	277	Mosquitoes and Malaria in Calcutta ..	473
		—as a Sequela of Recurrent Malaria (Talbot et al.) (C. T.) ..	428	The Annual Reports of the Lunatic Asylums of Bengal, Madras and the Punjab, for 1899 ..	518
		Erythroblastosis Foetalis (Allen et al.) (C. T.) ..	376	Lord Curzon on the Famine Mortality ..	572
		Erythrocyte, Infused, The Metabolic Fate of the (Levenson et al.) (C. T.) ..	429	Figueredo, N., see Bhende, Y. M., Purandare, N. M., Banker, D. D., and Desai, S. D. Outbreak of Kala-Azar in an Institution in Bombay (O. A.) ..	237
				Filarial Metamorphosis in the Anopheles (James) ..	326
				Filariasis, Bancroftian, with Hetrazan in British Guiana, Treatment of (Hewitt et al.) (C. T.) ..	528
				Findlay, G. M. Recent Advances in Chemotherapy, Vol. I ..	582
				Fischer, F. P., et al. Documenta Ophthalmologica—Advances in Ophthalmology, Vol. III ..	131
				Flocculation Tests in the Diagnosis of Hepato-Biliary Disease (Steigmann et al.) (C. T.) ..	224
				Floccillin '96', Experience with (Dutt and Bardhan) (O. A.) ..	199

	Page		Page		Page
Folic Acid Incompatibilities (C. T.)	30	Ghosh, S. M. Creeping Myiasis in Man (O. A.)	96	Harinasuta, C. Chloroquine in the Treatment of Amoebic Liver Abscess (O. A.)	37
—Acid, Liver Extract and, Combination of (Dey) (C.)	34	—S. M., and Mukherji, A. Cutaneous Amoebiasis (O. A.)	339	Hartridge, H. Recent Advances in the Physiology of Vision	582
—Acid and Neurologic Changes in Pernicious Anæmia (C. T.)	181	—T. N., see Bose, A. N., and Bose, S. Studies on Arsenoxide Derivatives, Part I (O. A.)	50	Head Lice, Gammexane in the Treatment of (C. T.)	426
—Acid, Pernicious Anæmia of Pregnancy, Successful Treatment with (Furman <i>et al.</i>) (C. T.)	576	Giles, H. McC., and other. Chloromycetin in Scrub-Typhus (C. T.)	274	Health Activities, Regional, W.H.O. Board Urges Development of (M. N.)	119
Food Poisoning, The Bacteriology of (Wilson) (C. T.)	127	Gipe, F. M., and other. Ward Administration and Clinical Teaching	131	—Care Needed by School-Age Children, W.H.O. Expert Group Defines Principles of (M. N.)	462
—Reserve, Vast Untapped, found in Central American Plants (C. T.)	524	Glaucoma, Treatment of (C. T.)	282	—Improvement in Asian Countries (M. N.)	267
Foreskin, The Fate of the (Gairdner) (C. T.)	276	Glycerine Vaccine Lymph, Penicillin Treatment of (Krishnamurthy) (C.)	283	—Machine Invention Cures Diverse Complaints (Lynch) (M. N.)	176
Franklin, J. R. Aureomycin in Infections of the Urinary Tract (C. T.)	179	Gokhale, B. B., and Ranade, S. N. Streptomycin in Syphilis (O. A.)	253	—Officer's Report, Calcutta Problems, Rural, in China (Tuckman) (C. T.)	574
Fuel Research Institute, President to Open (M. N.)	175	—G. N., and other. Plasma Protein Levels of Healthy Indian Subjects (C. T.)	377	—Standards, Ways to Raise (M. N.)	509
Fulton, J. F. Edited by—A Textbook of Physiology	229	—S. H., and Lokre, R. J. Some Constituents in Normal Blood in Central India (O. A.)	94	Heart Disease, Pain in the Chest Wall Simulating (Allison) (C. T.)	527
Furman, R. H., <i>et al.</i> Pernicious Anæmia of Pregnancy: Failure of Vitamin B ₁₂ Therapy: Successful Treatment with Folic Acid (C. T.)	576	Goldsmith, M. Cultivating Germs—To Produce Sulphur (M. N.)	510	—Failure, Congestive Cardiac, Mercurial Diuretics in (C. T.)	374
G		—Meteorites Bring News from Space (C. T.)	422	—Failure, Sudden (E.)	557
Gairdner, D. The Fate of the Foreskin (C. T.)	276	—Physicists Re-open the History Books (M. N.)	561	Hcaton, T. G. Artificial Pneumothorax in Pulmonary Tuberculosis	379
Gammexane in the Treatment of Head Lice (C. T.)	426	—Science and You (C. T.)	226	Helen Keller, Seventieth Birthday of (M. N.)	362
Gantrisin in the Treatment of Urinary Infections (Carroll <i>et al.</i>) (C. T.)	526	Gonorrhœa, Oral Administration of Aureomycin in the Treatment of (Chen <i>et al.</i>) (C. T.)	127	Heparin in Yellow Fever (Ahuja and other) (C.)	233
Garbled Quotation (Ross)	326	Gorin, N. Temporary Relief of Asthma by Jaundice (C. T.)	130	Hepatic Abscess, Pneumoperitoneum in the Study of (Lal) (O. A.)	90
Garcia, E. Y. Extract of Wings of Philippine Butterfly, <i>Terias hecabe</i> Linnaeus, New Antibiotic for Malaria (C. T.)	423	Gowin, E. L. D., <i>et al.</i> Blood Transfusion	529	Hepato-Biliary Disease, Flocculation Tests in the Diagnosis of (Seigmann <i>et al.</i>) (C. T.)	224
Garewal, A. S. I.M.G. Previous Issues (C.)	233	Graafand, A. C. H. Re: The Utrecht Fair, 1950 (M. N.)	367	Herbert, P., <i>et al.</i> Studies on the Effect of the Administration of Pituitary Adrenocorticotrophic Hormone (ACTH) to a Case of Loeffler's Syndrome and a Case of Tropical Eosinophilia (C. T.)	474
Garlick, H. W. Continuous Intra-gastric Drip in the Treatment of Peptic Ulcer (C. T.)	481	Gradwohl, R. B. H. Clinical Laboratory Methods and Diagnosis	82	Herpes Zoster with Aureomycin, Treatment of (Binder and other) (C. T.)	277
Garrod, L. P., and other. Hospital Outbreak of Enteritis due to Duck Eggs (C. T.)	278	Greval, S. D. S. Mushroom Poisoning in India (P. H. S.)	513	Hetrazan, Treatment of Bancroftian Filariasis with (Hewitt <i>et al.</i>) (C. T.)	528
Gastro-Enteritis, Acute, due to <i>T. vincenti</i> and <i>B. fusiformis</i> (Sanghvi and Subrahmanyam) (O. A.)	437	—S. D. S. Serological Technique: Immunotherapy (contd.) (O. A.)	453	Hewitt, R., <i>et al.</i> Follow-up Observations on the Treatment of Bancroftian Filariasis with Hetrazan in British Guiana (C. T.)	528
—Infantile, Chloramphenicol in Treatment of (Rogers <i>et al.</i>) (C. T.)	272	—S. D. S. Serological Technique: Immunotherapy (contd.) (O. A.)	554	Hiccup (C. T.)	80
Geriatric Medicine (E.)	209	Groundnut Cake Flour, Defatted, as Food (Lal and Bose) (P. H. S.)	322	Hill, A. B. Principles of Medical Statistics	283
Ghanem, M. H., and other. Clinical and Biochemical Studies in Cholera and the Rationale of Treatment (C. T.)	478	—Husk as Cattle Fodder (M. N.)	363	—C., and other. The National Health Service	131
Gharpure, P. V., and Jhala, H. I. The Relationship of the Body-Weight to the Weights of the Organs (O. A.)	342	Gupta, J. C., see Panja, D., and Banerji, A. K. Aureomycin in the Treatment of Pemphigus Foliaceus (M. H. P.)	503	Histoplasmosis and Tuberculosis (C. T.)	378
Ghosal, J. N. <i>Materia Medica, Pharmacology and Therapeutics, Parts I and II (In Bengali)</i>	380	—J. C., and Sen Gupta, P. C. Aureomycin in Kala-Azar (C.)	384	History Books, Physicists Re-open the (Goldsmith) (M. N.)	561
—S., see Chaudhuri, R. N., and Rai Chaudhuri, M. N. Chloromycetin in the Treatment of Cholera (O. A.)	398	—S. N. Paludrine Poisoning (C.)	433	Hoare, C. A. The Food Habits of <i>Entanaba histolytica</i> (C. T.)	474
Ghose, M. M. A Case of Acute Tingling (M. H. P.)	257	—S. N. Treatment of Cholera (C.)	584	Hoerr, S. O., <i>et al.</i> Clinical Evaluation of Various Tests for Occult Blood in the Faces (C. T.)	369
Ghosh, L. M., Dey, N. C., and Panja, D. Madura Foot (Mycetoma) (O. A.)	288	Gymnasium Aids Hospital Patients (M. N.)	115	Holzel, A., <i>et al.</i> Streptomycin Treatment of Infantile Diarrhoea and Vomiting (C. T.)	223
—P. K. An Outbreak of Plague in an Epidemic Form Treated with Streptomycin and Sulphadiazine (O. A.)	441	H		Homicide, Simulated (C. T.)	280
		Hæmatology, International Society of (M. N.)	174	Homœopathic Medical School	326
		Hæmiplegic Patient in General Practice, Physical Treatment of the (Dinken) (C. T.)	79	Hormones, The (E.)	159
		Hæmoglobin Determination, Blood Cell Counts and (C. T.)	374	Horne, G. O., and other. The Effect of Water and Salt Intake on Prickly Heat (C. T.)	277
		Hæmostatics, Absorbable (C. T.)	80	Hospital Bed, Featherlight (M. N.)	115
				Hospitals, British, Price Reductions Help (M. N.)	562

Page

Human Welfare, Science in Aid of (M. N.) ..

68

Hurst, A. A Twentieth Century Physician ..

431

Hyaluronidase in Pediatrics (C. T.) ..

273

Hydronephrotic Kidney, A Case of (Solanki) (M. H. P.) ..

402

Hydrophobia, Clinical, without Contact with Rabies Transmitting Animal (Brooks) (C.) ..

133

—Clinical, without Contact with Rabies Transmitting Animal (Deshmukhi) (C.) ..

483

—in India (Ahuja and Brooks) (O. A.) ..

449

Hydroxystillamidine in the Treatment of Indian Kala-Azar (Sen Gupta) (O. A.) ..

547

Hygiene in Indian Universities, The Teaching of ..

219

Hymenolepis diminuta in Man, A Case of Intestinal Infestation with (Parande) (M. H. P.) ..

256

Hyperplasia, Cystic, of the Human Breast, Squamous Metaplasia and Keratinization in (Rangam) (O. A.) ..

9

Hypertension, Chronic, Relief of, by Excision of Phenochromocytoma (Owens) (C. T.) ..

428

I

I.M.G. Previous Issues (Garewal) (C.) ..

233

Vaccines Minor (Das and Singh) (O. A.) ..

492

Index for Volume 84, 1949 (E.) ..

66

Indian Republic, The Birth of the (E.) ..

25

—Scientist Accepts High Post in W.H.O. (M. N.) ..

70

Industrial Medicine, The Second Annual All-India Conference of (M. N.) ..

406

Infantile Diarrhoea and Vomiting, Streptomycin Treatment of (Holzel et al.) (C. T.) ..

223

Infiltrations, Cave-Born Pulmonary, with Eosinophilia, Epidemic of (C. T.) ..

330

Insulin Resistance in Diabetes Patients (Bose) (O. A.) ..

445

Intragastic Drip, Continuous, in the Treatment of Peptic Ulcer (Garlick) (C. T.) ..

481

Intrathecal Medication, Dangers of (Wilson et al.) (C. T.) ..

125

Irani, R. J., see Pai, M. N. The Antibacterial Principle of the Betel Leaf (O. A.) ..

302

Iron Hamatoxylin Stain for Protozoa in Tissue Sections and Smears, A Rapid Method of (Sen Gupta et al.) (O. A.) ..

400

Isopropylpinephrine and Bronchial Asthma (C. T.) ..

126

J

Jain, K. D. A Case of Cerebral Malaria (M. H. P.) ..

403

James, S. P. Filarial Metamorphosis in the Anopheles ..

326

Jomieson, E. M., and other. Trends in Nursing History ..

82

Jennings, C. H. Protracted Nervous Complications of Typhoid Fever (C. T.) ..

275

Jhala, H. I., see Gharpure, P. V. The Relationship of the Body-Weight to the Weights of the Organs (O. A.) ..

342

Page

Johansen, F. A., et al. Proniacetin in Treatment of Leprosy (C. T.) ..

522

Jolly, H. W., and other. The Management of Acne in General Practice (C. T.) ..

425

Joseph, P. A. P., see Cooray, G. H. A Case of Xeroderma Pigmentosa in a Sinhalese (M. H. P.) ..

101

Joshi, N. V. Indian Curds or 'Dahi' as a Source of Vitamin B Complex and Growth Factors (C. T.) ..

376

Journal of Bone and Joint Surgery (M. N.) ..

366

K

Kagan, B. M., et al. Chorea (Sydenham) : A Study of Fifty-eight Additional Patients (C. T.) ..

225

Kala-Azar, Aureomyces in (Gupta and Sen Gupta) (C.) ..

384

—in India and the Sandfly (Bouche) (C.) ..

534

—in India and the Sandfly (Brooks) (C.) ..

380

—Indian, Hydroxystillamidine in the Treatment of (Sen Gupta) (O. A.) ..

547

—in an Institution in Bombay, Outbreak of (Bhende et al.) (O. A.) ..

237

—A New Method of Diagnosis (Raghavan) (C. T.) ..

475

—Relapse following Splenectomy (Morton) (C. T.) ..

475

—Treatment of, with Methyl Glucamine Antimoniate (Sen Gupta) (O. A.) ..

291

Kalra, S. L., see Narain, S. Streptomycin in Tick-borne Relapsing Fever of Kashmir (O. A.) ..

87

Kamalapur, K. S., and other. The 11th Maharashtra and Karnatak Provincial Medical Conference, Dharwar (M. N.) ..

116

Kamath, M. V., see Thomas, T. Oral Novocaine Therapy in Peptic Ulcer (O. A.) ..

16

Kant, L., see Rudra, M. N. A Field Investigation into Lathyrism (P. H. S.) ..

415

Kaplan, S. R., et al. Healed Subacute Bacterial Endocarditis (C. T.) ..

182

Kapoor, S. C., see Samad, A. A Case of Acute Nephritis Treated with an Antihistaminic Drug (M. H. P.) ..

208

Kapur, K. B., and Das Gupta, P. R. Sexual Disorder in 'Mepacrine Psychoses' (M. H. P.) ..

20

Keegan, D. F. Our Special Number ..

368

Keith, M. M., and other. Clinical Intoxication with Potassium (C. T.) ..

124

Keller, Dr. Helen, Seventieth Birthday of (M. N.) ..

362

Kersley, G. D. The Rheumatic Diseases ..

528

Khambatta, S. M.D. and M.S., Bombay (C.) ..

133

Khan, N. Comparative Value of Sulphadiazine and Sulpha-guanidine in the Treatment of Acute Bacillary Dysentery (O. A.) ..

490

Khanna, H., see Singh, B. Muscular Anomalies (O. A.) ..

391

Kilham, L. Mumps Meningoencephalitis with and without Parotitis (C. T.) ..

225

Kini, M. G., and Naidu, I. C. Cup Arthroplasty in Hip Joint Surgery (O. A.) ..

19

Kinnear, N. The Last Twenty Years of Abdominal Surgery (C. T.) ..

577

Kippen, G. S., and other. Early and Delayed Clinical Effects of Vagotomy for Peptic Ulcer (C. T.) ..

427

Kiskadden, W. S., et al. Theories of the Etiology of Congenital Deformities (C. T.) ..

223

Kitchen, New Tool for the (C. T.) ..

30

Kleiner, I. S. Human Biochemistry ..

81

Koch and Cholera (M. N.) ..

512

Konar, N. R. Pneumococcal Meningitis with Atypical Features (O. A.) ..

245

N. R., and Banerjee, D. Disseminated Lupus Erythematosus (O. A.) ..

188

N. R., and Das, A. K. Barbiturate Poisoning Treated with PicROTOXIN (O. A.) ..

494

Koos, E. L. The Sociology of the Patient ..

582

Kordy, M. I. E. A Simple New Stain for Intestinal Protozoa (C. T.) ..

181

Koshly, P. Amœbic Abscess of the Brain (O. A.) ..

287

Kothare, S. N., see Bhende, Y. M. Aneurysmal Bone Cyst (O. A.) ..

544

Kothari, B. V., and other. Nutritional Megaloblastic Anæmia : So-called Pernicious Anæmia of Pregnancy (C. T.) ..

422

Kothavala, Z. R. International Honour for Indian Scientist (M. N.) ..

28

Krishnamurthy, V. N. Penicillin Treatment of Glycerine Vaccine Lymph (C.) ..

283

Krishnan, K. V., Chaudhuri, R. N., Chakravarti, H., and Rai Chaudhuri, M. N. Aureomycin in the Treatment of Typhoid, Typhus, Cystitis and Pertussis (O. A.) ..

202

L

L.T.M. Examination Results, Session 1950 (M. N.) ..

512

Labelling Provisions under Drugs Act (M. N.) ..

176

Lal, H. B. Pneumoperitoneum in the Study of Hepatic Abscess (O. A.) ..

90

—R. B. A 'New Latrine,' Suitable for Rural Communities, Camps and Isolated Bungalows (P. H. S.) ..

469

—S. B., and Bose, A. Use of Defatted Groundnut Cake Flour as Food (P. H. S.) ..

322

Lane, C. G. Roentgen Rays in the Treatment of Cutaneous Diseases (C. T.) ..

580

Lathyrism, A Field Investigation into (Rudra and Kant) (P. H. S.) ..

415

Latrine, New, Suitable for Rural Communities (Lal) (P. H. S.) ..

469

Laurence-Moon-Bardet-Biedl Syndrome (Rao) (O. A.) ..

542

Lavi, R. G. Ophthalmological Journals (A. Q.) ..

434

Lawrence, J. N., et al. Radioactive Phosphorus in Chronic Lymphatic Leukæmia (C. T.) ..

522

Page		Page		Page	
			M		
Leper Mission in India, Work of (M. N.)	270	M.D. and M.S., Bombay (Khambatta) (C.)	133	McLester, J. S. <i>Nutrition and Diet in Health and Disease</i> ..	481
Leprosy with Diamino-Diphenyl Sulphone by Mouth, Treatment of (Lowe) (C. T.)	275	Mackenzie, I. Somatic Movements of the Prematurely Born Fetus (C. T.)	180	McSwain, B., <i>et al.</i> Ewing's Tumour (C. T.)	122
Experimental Work with the Sulphone Group in (C. T.)	370	Madness, Myxoedematous (Asher) (C. T.)	222	Measles Encephalitis (Sawchuk <i>et al.</i>) (C. T.)	375
in Fakfak, Drug for (M. N.)	409	Madura Foot (Mycetoma) (Ghosh <i>et al.</i>) (O. A.)	288	Medical Conference, The 16th Andhra Provincial (M. N.)	70
The Present Status of Sulphones in the Treatment of (Dharmendra) (S. A.)	348	Majumder, N., <i>see</i> Subrahmanyam, K. Efficiency of Settling Tanks in Two Water Purification Plants in India (P. H. S.)	565	Conference, 27th All-India (M. N.)	411
Promacetin in Treatment of (Johansen <i>et al.</i>) (C. T.)	522	Malaria, Acute, the Dosage of Quinine to be Administered in (Winckel) (C. T.)	576	Conference, 9th Bengal Provincial (M. N.)	69
Tamed (E.)	347	A Case of Sciatica due to (Wahi) (M. H. P.)	255	Conference, Dharwar, The 11th Maharashtra and Karnatak Provincial (Kamalapur and other) (M. N.)	116
Training Course (M. N.)	212	Cerebral, A Case of (Jain) (M. H. P.)	403	Correspondence College (Dutta) (C.)	34
Leukæmia, Chronic Lymphatic, Radioactive Phosphorus in (Lawrence <i>et al.</i>) (C. T.)	522	Chlorguanide Hydrochloride and (C. T.)	526	Council, United Provinces, Lucknow, Minutes of the Meeting of (Banerjee) (M. N.)	113
Levenson, S. M., <i>et al.</i> The Metabolic Fate of the Infused Erythrocyte (C. T.)	429	Chronic Vivax, with Pentaquine, Cure of (Coggeshall and other) (C. T.)	122	Council, Uttar Pradesh (Bajpayee) (M. N.)	362
Life, Man's Expectation of, 'Considerably Increased' (M. N.)	460	Control in the British Colonies (M. N.)	118	Forum, Indian (M. N.)	365
Life-Span, Human, Doubling in Next 10 Years Possible (C. T.)	525	Control in Ceylon (M. N.)	257	Experts Advise on Training (M. N.)	111
Linseed Straw to Replace Jute (M. N.)	363	Extract of Wings of Philippine Butterfly, <i>Terias hecabe</i> Linnaeus, New Antibiotic for (Garcia) (C. T.)	423	Journals, A Note on Filing (Deshmukh) (C.)	284
Liver Disease, Amœbic Dysentery and (Chakravarti) (O. A.)	394	Falciparum, with Intramuscular Chloroquine, The Treatment of (Spicknall <i>et al.</i>) (C. T.)	476	Officers of Schools Association, Issued by Handbook of Communicable Diseases for the Use of Medical Officers of Schools	481
Extract and Folic Acid, Combination of (Dey) (C.)	34	and Malaria Control Measures (Viswanathan) (C. T.)	376	Research Council: Special Report Series No. 264, 1949—Vitamin A Requirement of Human Adults	331
Infantile Cirrhosis of the, Treatment of (Rao) (O. A.)	150	Mosquitoes and, in Calcutta	473	Research Council: Special Report Series No. 266: Infection and Sepsis in Industrial Wounds of the Hand	582
Infantile Cirrhosis of the, Treatment of (Singh) (C.)	531	Primary and Relapsing (Patwa) (A. Q.)	184	Supplies to S.-E. Asian Countries, by W.H.O. (M. N.)	367
Post-Necrotic Scarring of the, in a Child and its Possible Relationship to Rh Factor (Tribedi and Chanda) (O. A.)	192	Rate Reduced in Area of Pakistan Spread in Project of W.H.O. and U.N. Children's Fund (M. N.)	461	Union, Bombay (M. N.)	363
Loeffler's Syndrome and a Case of Tropical Eosinophilia, Studies on the Effect of the Administration of Pituitary Adrenocorticotrophic Hormone to a Case of (Herbert <i>et al.</i>) (C. T.)	474	Recurrent, Epilepsy as a Sequela of (Talbot <i>et al.</i>) (C. T.)	277	Medicinal Plant, British Expedition's Search for (M. N.)	25
Lokre, R. J., <i>see</i> Gokhale, S. H. Some Constituents in Normal Blood in Central India (O. A.)	94	Recurrent, Epilepsy as a Sequela of (Talbot <i>et al.</i>) (C. T.)	428	Medicine Spoons (M. N.)	363
London Letter	421	Splenomegaly, The Effect of Chloroquine Diphosphate on (Berberian and other) (C. T.)	128	Mehta, C. M. An Appeal (C.)	233
Low, R. C., and other. <i>Common Diseases of the Skin</i>	429	Studies on Plasma Protein (Chakravarti) (O. A.)	500	R. D. Cholera in Hyderabad State (P. H. S.)	569
Lowe, J. Treatment of Leprosy with Diamino-Diphenyl Sulphone by Mouth (C. T.)	275	Successful Campaign, Cyprus Freed from (C. T.)	424	Melena (Thompson and other) (C. T.)	369
Low-Salt Diet in Treatment of Hypertension and Hypertensive Heart Disease (Bang <i>et al.</i>) (C. T.)	273	Treatment of (Dani) (C.)	33	Mellanby, Sir Edward (M. N.)	314
Lunatic Asylums of Bengal, Madras and the Punjab for 1899	518	Malhotra, S. L. Gonococcal Arthritis (O. A.)	187	Meningitis, Pneumococcal, with Atypical Features (Konar) (O. A.)	245
Lung Abscess by Inhalation of Micropulverized Penicillin, Treatment of a (O'Driscoll) (C. T.)	273	Malnutrition and Starvation (C. T.)	576	Tubercular, 'Positive Cure' Claimed for (C. T.)	227
'Dusted', Menace of the (Bramhall) (M. N.)	265	Mammary Carcinoma (Ray) (S. A.)	66	'Mepacrine Psychoses', Sexual Disorder in (Kapur and Das Gupta) (M. H. P.)	20
Lungs, Multiple Amœbic Abscess of the (Chatterjee and other) (C. T.)	281	Marriott, H. L. A Simple Weight-Reducing Diet (C. T.)	123	Mercurial Diuretics in Congestive Cardiac Heart Failure (C. T.)	374
Lupus Erythematosus, Disseminated (Konar and Banerjee) (O. A.)	188	Maternal and Child Health (M. N.)	27	Metaphysial Aclasis (Berry) (O. A.)	387
Lymphocele of the Scrotum, An Unusual Case of (Tribedi) (M. H. P.)	256	Maternity and Child Welfare Work in Railway Colonies (Chopra) (P. H. S.)	317	Meteorites Bring News from Space (Goldsmith) (C. T.)	422
Lymphosarcoma, Mediastinal, in a Child (Mukerjee) (M. H. P.)	206	Maxillary Incisors, The Nerve Supply to the (Cook) (C. T.)	521	Methyl Glucamine Antimoniate, Treatment of Kala-Azar with (Sen Gupta) (O. A.)	291
Lynch, C. Health Machine Invention Cures Diverse Complaints. Australian Apparatus Expedites Blood Circulation and Tones Up System (M. N.)	176	Maximow, A. A., and other. <i>Textbook of Histology</i>	331	Glucamine Antimoniate, Urinary Excretion of Antimony after Administration of (Chakravarti and Sen Gupta) (O. A.)	388
		McCormick, W. J. Poliomyelitis: Infectious or Metabolic? (C. T.)	579	Micks, R. H. <i>The Essentials of Materia Medica, Pharmacology and Therapeutics</i>	581
				Microfilm Service Unit, Indian Council of Medical Research (M. N.)	311
				Miller, A. Management of Anuria (C. T.)	377

Page		Page		Page	
Mitchell-Heggs, G. B. Tenth International Congress of Dermatology (M. N.)	558	Narain, B. Nutrition	81	Ozena, Streptomycin Treatment of (Simontou) (C. T.)	281
Mitra, S. K., see Sen Gupta, A. An Observation on Preserved Ova of Ascaris Lumbricoides (O. A.)	138	S., and Kalra, S. L. Streptomycin in Tick-Borne Relapsing Fever of Kashmir (O. A.)	87	P.	
Mohanty, J. K., and Pabrai, P. R. Studies on Sex Hormones, Part I (O. A.)	43	National Association for the Prevention of Tuberculosis—Tuberculosis Index and Abstracts of Current Literature	130	Pabrai, P. R., see Mohanty, J. K. Studies on Sex Hormones, Part I (O. A.)	43
Monilia Infection, Perionychia due to (Panja and Banerjee) (O. A.)	137	Nephritis Acute, Treated with an Antihistamine Drug, A Case of (Samad and Kapoor) (M. H. P.)	208	Pai, M. N., and Irani, R. J. The Antibacterial Principle of the Betel Leaf (O. A.)	302
Moniliasis, Pulmonary (Singh) (O. A.)	10	Newton, W. H. Recent Advances in Physiology	282	Paludrine Poisoning (Dutta) (C.)	533
Morgan, H. The	229	Nicotinic Acid in Diabetic Patients, Studies of the Urinary Excretion of (Rindani and Rao) (O. A.)	488	Paludrine Poisoning (Gupta) (C.)	433
Advances in the Study of Venereal Disease (C. T.)	425	Night Cramps and Quinine (C. T.)	581	Poisoning, Accidental, A Case of (Sen) (M. H. P.)	305
Morton, T. C. Kala-Azar: Relapse following Splenectomy (C. T.)	475	Nitrogen Mustard Hydrochloride (M. N.)	367	Pan-American Sanitary Bureau (M. N.)	361
Mosquito Bites, Severe Generalized Reaction to (Crewe and other) (C. T.)	377	Nobel Festival (M. N.)	366	Pandalai, N. G. A Textbook of Bacteriology	482
Malaria, Recent Italian Work on	119	Notes on Some Remedies. XXXII. Dehydration and its Treatment, Part IV (Chaudhuri) (T. N.)	57	Pandit, S. R. Two Instances of Proved Rabies in the Tiger (O. A.)	441
Mosquitoes and Malaria in Calcutta	473	XXXIII. Dehydration and its Treatment, Part IV (contd.) (Chaudhuri) (T. N.)	105	Panja, D., and Banerjee, A. K. Perionychia due to Monilia Infection (O. A.)	137
Motion Sickness (C. T.)	281	XXXIV. Dehydration and its Treatment (Chaudhuri) (T. N.)	257	D., see Ghosh, L. M., and Dey, N. C. Madura Foot (Mycetoma) (O. A.)	288
Mukherjee, A. B. Mediastinal Lymphosarcoma in a Child (M. H. P.)	206	Nott, A. H. The Value of 'Sags' as Antiscorbutics in the Jail Dietary	327	D., Gupta, J. C., and Banerji, A. K. Aureomycin in the Treatment of Pemphigus Foliaceus (M. H. P.)	503
D. N. Leprosy: Facts and Fiction	332	Novocaine Therapy, Oral, in Peptic Ulcer (Thomas and Kamath) (O. A.)	16	D., see Sen Gupta, P. C., and Banerjee, A. K. An Unusual Case of Post-Kala-Azar Dermal Leishmaniasis (O. A.)	138
I. B. Advertisements in Medical Journals (C.)	434	Nuffield Foundation Travelling Fellowships Awards to Indian Graduates (Farrer-Brown) (M. N.)	468	Para-Aminosalicylic Acid (C. T.)	129
S. K. Rheumatoid Arthritis in a Child with Unusual Manifestations (O. A.)	247	Nurses, World-Wide Shortage of, W.H.O. Experts Recommend Measures in (M. N.)	112	Acid: PAS (E.)	107
Mukherji, A., see Ghosh, S. M. Cutaneous Amebiasis (O. A.)	339	Nutrition, Parenteral, in the Surgical Patient as Provided from Glucose, Amino Acids and Alcohol (Rice et al.) (C. T.)	520	Acid (P.A.S.) in Pulmonary Tuberculosis (Nagley and other) (C. T.)	79
Mumps Meningoencephalitis with and without Parotitis (Kilham) (C. T.)	225	Nylon Dressing for Wounds, The New Surgical (M. N.)	265	Acid and Streptomycin, Treatment of Pulmonary Tuberculosis with (C. T.)	272
Murthy, V. N. K. Toxic Factor(s) in Vaccinia Virus and its Neutralization by Penicillin (O. A.)	487	O		Paracholera (C. T.)	126
Muscular Anomalies (Singh and Khanna) (O. A.)	391	Obituaries of Physicians in U.S.A. (M. N.)	365	Parande, A. S. A Case of Intestinal Infestation with <i>Hymenolepis diminuta</i> in Man (M. H. P.)	256
Museum, Clinical Pathological, in Medical Education, the Place of (Wahi and Samuel) (O. N.)	54	Occult Blood in the Faeces, Various Tests for (Hoerr et al.) (C. T.)	369	Paratyphoid Fever, Typhoid and, Chloromycetin in (Treu) (O. A.)	154
Mushroom Poisoning in India (Grevil) (P. H. S.)	513	O'Driscoll, D. T. Treatment of a Lung Abscess by Inhalation of Micropulverized Penicillin (C. T.)	273	Parkinsonism, Artane Therapy for (Doshay and other) (C. T.)	276
Musick, V. H., et al. A Simplified Caffeine Gastric Test Meal for the Diagnosis of Peptic Ulcer (C. T.)	278	Ophthalmic Diseases, Certain, Typhoid Vaccine in Treatment of (Curry and other) (C. T.)	224	Paryphostomum sufraginifer (Intestinal Fluke) Infection in Man (Reddy and Varmah) (O. A.)	546
Mustard Seeds, Argemone and (Sanyal) (O. A.)	498	Ophthalmological Journals (Lavi) (A. Q.)	434	Pastore, A. R. Brazil's Snake Farm (M. N.)	361
(Mycetoma) Madura Foot (Ghosh et al.) (O. A.)	288	Orr, T. G. Operations of General Surgery	131	Pathological Research, New Machine for (M. N.)	562
Myelosclerosis (C. T.)	222	Oslo School Breakfast (Sachs) (C. T.)	328	Patwa, C. M. Primary and Relapsing Malaria (A. Q.)	184
Myiasis, Creeping, in Man (Ghosh) (O. A.)	96	Our Special Number (Keegan)	368	Payne, E. H., et al. Pertussis Treated with Chloramphenicol (C. T.)	424
Of the Nasal Cavity, A Case of (Bhowmick) (M. H. P.)	306	Overman, W. E. Penicillin and Black Hairly Tongue (C. T.)	423	Pediatrics, Hyaluronidase in (C. T.)	273
'Myoidema' and 'Myotatic Irritability' (Deshmukh) (O. A.)	197	Owens, F. M. Relief of Chronic Hypertension by Excision of Pheochromocytoma (C. T.)	428	Pemphigus Foliaceus, Aureomycin in the Treatment of (Panja et al.) (M. H. P.)	503
'Myotatic Irritability', 'Myoidema' and (Deshmukh) (O. A.)	197			Penicillin and Black Hairly Tongue (Overman) (C. T.)	423
N				in Human Milk, The Excretion of (Rozansky and other) (C. T.)	31
Nagley, M. M., and other. Para-Aminosalicylic Acid (P.A.S.) in Pulmonary Tuberculosis (C. T.)	79			Micropulverized, Treatment of a Lung Abscess by Inhalation of (O'Driscoll) (C. T.)	273
Naidu, I. C., see Kini, M. G. Cup Arthroplasty in Hip Joint Surgery (O. A.)	19				
Nalish, J. M., and other. The Clinical Apprentice	130				

	Page		Page		Page
Penicillin, Oral Reactions to (Cross) (C. T.) ..	31	Plague (Blanc) (M. N.) ..	69	Pregnancy, Submucous Fibroid Simulating (Bhadury) (M. H. P.) ..	345
— in Reducing Bacterial Contamination in Vaccine Lymph, Efficacy of (Das Gupta) (P. H. S.) ..	514	— in an Epidemic Form Treated with Streptomycin and Sulphadiazine, An Outbreak of (Ghosh) (O. A.) ..	441	Press Information Bureau, Government of India (M. N.) ..	316
— and Streptomycin on <i>Endanaba histolytica</i> Cultures, Synergistic Action of (Seneca <i>et al.</i>) (C. T.) ..	125	— Can be Eradicated by the Expert Adviser on Plague (M. N.) ..	173	— Note (M. N.) ..	460
— and Sulphadiazine in Lobar Pneumonia (Chatterjee) (C.) ..	233	— Pneumonic, Precautionary Measures in the Management of (Dalal) (C.) ..	284	Price, A. L. <i>The American Nurses' Dictionary</i> ..	81
— Toxic Factor(s) in Vaccinia Virus and its Neutralization by (Murthy) (O. A.) ..	487	Plasma Protein Levels of Healthy Indian Subjects (Gokhale and other) (C. T.) ..	377	Prickly Heat, The Effect of Water and Salt Intake on (Horne and other) (C. T.) ..	276
— Treatment of Glycerine Vaccine Lymph (Krishnamurthy) (C.) ..	283	— Protein, Studies on. I. Kala-Azar (Chakravarti) (O. A.) ..	141	Procaine Penicillin with Aluminium Monostearate (Robinson) (C. T.) ..	224
— Treatment, A Single, Is Syphilis Curable with (M. N.) ..	559	— Protein, Studies on. II. Amœbic Dysentery and Liver Disease (Chakravarti) (O. A.) ..	394	— Penicillin with Aluminium Monostearate, The Use in Children of (Emery <i>et al.</i>) (C. T.) ..	123
Pentaquine, Cure of Chronic Vivax Malaria with (Coggeshall and other) (C. T.) ..	122	— Protein, Studies on. III. Malaria (Chakravarti) (O. A.) ..	500	Proguanil, Resistance to (C. T.) ..	519
Pepper, O. H. P. <i>Medical Etymology</i> ..	228	Plastics, New Uses for (Williams) (M. N.) ..	314	Promacetin in Treatment of Leprosy (Johansen <i>et al.</i>) (C. T.) ..	522
Peptic Ulcer, Continuous Intra-gastric Drip in the Treatment of (Garlick) (C. T.) ..	481	Pneumolysis, Closed Intrapleural, Empyema following (Dingley) (O. A.) ..	337	Protozoa, Intestinal, A Simple New Stain for (Kordy) (C. T.) ..	181
— Ulcer, Early and Delayed Clinical Effects of Vagotomy for (Kipen and other) (C. T.) ..	427	Pneumonia, Lobar, Penicillin and Sulphadiazine in (Chatterjee) (C.) ..	233	Pruritus Vulvæ, Sodium Propionate in the Treatment of (C. T.) ..	427
— Ulcer, Oral Novocaine Therapy in (Thomas and Kamath) (O. A.) ..	16	— Primary Atypical, Antibiotics in (C. T.) ..	124	Psoriasis, Peroral Administration of Undecylenic Acid in (Perlman and other) (C. T.) ..	125
— Ulcer, A Simplified Caffeine Gastric Test Meal for the Diagnosis of (Musick <i>et al.</i>) (C. T.) ..	278	Pneumo-Peritoneum, Spontaneous (Dingley) (O. A.) ..	492	Purandare, N. M., <i>see</i> Bhende, Y. M., Banker, D. D., Figueredo, N., and Desai, S. D. Outbreak of Kala-Azar in an Institution in Bombay (O. A.) ..	237
Perionychia due to Monilia Infection (Panja and Banerjee) (O. A.) ..	137	— in the Study of Hepatic Abscess (Lal) (O. A.) ..	90		
Perlman, H. H., and other. Peroral Administration of Undecylenic Acid in Psoriasis (C. T.) ..	125	Points from a Letter (Chatterji) (C.) ..	584	Q	
Pertussis and Aureomycin (Beel <i>et al.</i>) (C. T.) ..	220	Poland Announces Decision to withdraw from W.H.O. (M. N.) ..	462	Q Fever in London, Outbreak of (M. N.) ..	118
— Treated with Chloramphenicol (Payne <i>et al.</i>) (C. T.) ..	424	Polio : Two New Points (E.) ..	558	Quackery Charges Against Six Medical Practitioners (M. N.) ..	561
— Typhoid, Typhus, Cystitis, and Aureomycin in the Treatment of (Krishnan <i>et al.</i>) (O. A.) ..	202	— Yet Again (E.) ..	108	Quarantine Restrictions (M. N.) ..	116
Pharmaceutical Congress, Indian (M. N.) ..	467	Poliomyelitis, Acute, Symptom Complex in (Smith <i>et al.</i>) (C. T.) ..	375	— Restrictions (M. N.) ..	367
— Society of Great Britain—Published by—The British Pharmaceutical Codex, 1949 ..	227	— Anterior, Use of Curare in the Treatment of (Bower <i>et al.</i>) (C. T.) ..	580	— Restrictions (M. N.) ..	406
Pharmacopœia, International, Progress Towards an (M. N.) ..	26	— Declining after Summer Outbreaks (M. N.) ..	558	Quinine to be Administered in Acute Malaria, the Dosage of (Winckel) (C. T.) ..	576
Photography, Medical (M. N.) ..	174	— Infectious or Metabolic? (McCormick) (C. T.) ..	579	— Night Cramps and (C. T.) ..	581
Physical Medicine Department, Most Modern (M. N.) ..	116	— and Tonsillectomy (C. T.) ..	222		
— Therapy Journals (Bhatt) (A. Q.) ..	334	Pollution of Ground Water from Borehole Latrines, The Risk of (Subrahmanyam and Bhaskaran) (P. H. S.) ..	418	R	
Physicians of India, Association of (M. N.) ..	70	Ponsford, L. G. Ross Institute of Tropical Hygiene : Course in Tropical Hygiene for Planters and Miners (M. N.) ..	263	Rabies (E.) ..	457
Picrotoxin, Barbiturate Poisoning Treated with (Konar and Das) (O. A.) ..	494	Population Institute, India Sets Up (M. N.) ..	108	— Conference, Caribbean, Recommends Co-ordination of Rabies Control in Area (M. N.) ..	463
Pillay, A. P. <i>Disorders of Sex and Reproduction</i> ..	482	Post-Graduate Medical Studies, Facilities for (M. N.) ..	468	— in the Tiger, Two Instances of (Pandit) (O. A.) ..	441
Pinworm Diagnosis, Methods of (Beaver) (C. T.) ..	128	Potassium, Clinical Intoxication with (Keith and other) (C. T.) ..	124	Radio-Active Isotopes, Record Production of (M. N.) ..	311
Pituitary Adrenocorticotrophic Hormone to a Case of Loeffler's Syndrome and a Case of Tropical Eosinophilia, Studies on the Effect of the Administration of (Herbert <i>et al.</i>) (C. T.) ..	474	— Permanganate in the Disinfection of Water, The Use of (Banerjee) (P. H. S.) ..	214	Radiology, Congress of (M. N.) ..	270
		Pottenger, F. M. <i>Tuberculosis</i> Pramanik, S. Reiter's Disease (M. H. P.) ..	379	Raghavan, N. G. S. A New Method of Diagnosis of Kala-Azar (C. T.) ..	475
		Precision Instruments under Construction in Delhi Laboratory (M. N.) ..	312	Rai Chaudhuri, M. N., <i>see</i> Chaudhuri, R. N., and Ghosal, S. Chloromycetin in the Treatment of Cholera (O. A.) ..	398
				— M. N., <i>see</i> Krishnan, K. V., Chaudhuri, R. N., and Chakravarti, H. Aureomycin in the Treatment of Typhoid, Typhus, Cystitis and Pertussis (O. A.) ..	202
				Rauade, S. N., <i>see</i> Gokhale, B. B. Streptomycin in Syphilis (O. A.) ..	253
				Rangam, C. M. Squamous Metaplasia and Keratinization in Cystic Hyperplasia of the Human Breast (O. A.) ..	9

Page		Page		Page	
Rao, G. S. Brief Notes on Two Cases of Scrub Typhus Fever with Unusual Neurological Signs (M. H. P.)	103	Annual Report on Civil Hospitals and Dispensaries in the Central Provinces and Berar, 1946	232	Leprosy: Facts and Fiction (Mukherjee)	332
— G. S. Typhus in the Northern Circars (C.)	33	— Report of the Tuberculosis Relief Association	332	Materia Medica, Pharmacology and Therapeutics, Parts I and II (In Bengali) (Ghosal)	380
— K. N. A., and other. Tick-Borne Relapsing Fever in Kashmir (C. T.)	128	P. G. Singhanee Hindu Hospital, Bombay	333	— Medica, Pharmacology and Therapeutics, The Essentials of (Micks)	581
— K. S. The Laurence-Moon-Bardet-Biedl Syndrome (O. A.)	542	Report of the Scientific Advisory Board, I.R.F.A., 1949	432	Medical Annual, 1950, the (Tidy)	581
— P. K. Treatment of Infantile Cirrhosis of the Liver (O. A.)	150	The Thirty-second Annual Report of King Edward VII Memorial Pasteur Institute and Medical Research Institute, Shillong, 1948	530	Medicine, Applied (Beaumont)	430
— P. K. Treatment of Infantile Cirrhosis of the Liver (C.)	531, 532	Annual Report of the Chemical Examiner's Department, Madras, 1949	531	— Clinical, Normal Values in (Sunderman and other)	283
— S. N. N., see Rindani, T. H. Studies of the Urinary Excretion of Nicotinic Acid in Diabetic Patients (O. A.)	488	Indian Association for the Cultivation of Science	583	— Lectures on, to Nurses (Clark-Kennedy)	379
Ray, H. N. Echinococcal Cyst of Broad Ligament (O. A.)	88	Research, Organizations for	77	— Ophthalmic (Doggart)	132
— Dr. K. S. (E.)	558	Rovlows.		— Psychosomatic (Weiss and other)	228
— P. N. Mammary Carcinoma (S. A.)	66	Allergy, Practice of (Vaughan)	227	Midwifery (Brown and Dobbs)	581
— S. N. Sudden Death of Babies (C.)	133	Amputations, An Atlas of (Slocum)	131	— A Textbook of (Shaw)	130
Raynaud's Disease, Effect of Fibrinolytic and Anti-Thyroidin on (Datta and Thakurta) (M. H. P.)	102	Apprentice, The Clinical (Naish and other)	130	Motherhood, Introduction to (Read)	581
Read, G. D. Introduction to Motherhood	581	Artificial Pneumothorax in Pulmonary Tuberculosis (Heaton)	379	Nervous System, The Clinical Examination of the (Mourad-Krohn)	229
Red Cross Exhibition, London (M. N.)	114	Bacteriology, Textbook of (Burrows)	332	Nurses, Lectures on Medicine to (Clark-Kennedy)	379
Reddy, D. G., and Varmah, K. <i>Paryphostomum sufraginifer</i> (Intestinal Fluke) Infection in Man (O. A.)	546	— A Textbook of (Pandalai)	482	Nursing History, Trends in (Janusson and other)	82
Register of Scientific Personnel (M. N.)	265	Biochemistry, Human (Kleiner)	81	Nutrition (Narain)	81
Reiter's Disease (Pramanik) (M. H. P.)	304	Blood Transfusion (Gowin <i>et al.</i>)	529	— and Diet in Health and Disease (McLester)	481
Relapsing Fever, Tick-Borne, in Kashmir (Rao and Kalra) (C. T.)	128	British P.	529	Obstetric Analgesia and Anaesthesia (Snyder)	282
— Fever, Tick-Borne, of Kashmir, Streptomycin in (Narain and Kalra) (O. A.)	87	Society	227	Obstetrics and Diagnostic Gynaecology, Handbook of (Doyle)	430
Renal Calculus (Winsbury-White) (C. T.)	278	Cancer, radiotherapy and (Taylor <i>et al.</i>)	81	— and Gynaecology, A Synopsis of (Bourne)	32
Reports (Abstracts).		Cardiovascular Disease in General Practice (East)	130	Operations of General Surgery (Orr)	131
Annual Report of the Chemical Examiner's Department, Madras, 1948	33	Chemist	379	Ophthalmic Medicine (Doggart)	132
— Report of the Director of the Pasteur Institute of Southern India, Coonoor, together with the Forty-second Annual Report of the Central Committee of the Pasteur Institute Association, 1948-49	83	of (A.)	582	Ophthalmologica, Documenta—Advances in Ophthalmology, Vol. III (Fischer <i>et al.</i>)	131
Drug Standardization in India: Report of the Government Laboratory	83	Chemotherapy, Recent Advances in, Vol. I (Findlay)	582	Ophthalmology, Advances in—Documenta Ophthalmologica (Fischer <i>et al.</i>)	131
Annual Report on the Health of the Army in India, 1947	184	Communicable Diseases, Handbook of (Medical Officers' Schools Association)	481	— Textbook of, Vol. IV (Duke-Elder)	182
— Report on the Working of the Assam Mental Hospital, Tezpur, 1948	229	Current Therapy (Cohn <i>et al.</i>)	431	Pædiatrics, Synopsis of (Zahorsky)	130
The 83rd Annual Report of the Chemical Examiner to the Government, United Provinces, 1947	230	Cytology, General (Robertis <i>et al.</i>)	228	Pathology (Anderson)	331
Administration Report of K. E. M. Hospital and G. S. M. College, 1948-49	231	Dictionary, Nurses', the American (Price)	81	Patient, The Sociology of the (Koo)	582
Brief Report on Hospitals and Dispensaries, Central Provinces and Berar, 1941-45, together with Annual Report, 1946	232	Diet, Nutrition and, in Health and Disease (McLester)	481	Perimetry, Clinical (Traquair)	132
		Etymology, Medical (Pepper)	228	Pharmacology, Materia Medica and Therapeutics, Parts I and II (In Bengali) (Ghosal)	380
		Eye Manifestations of Internal Diseases, The (Tassman)	331	Physician, A Twentieth Century (Hurst)	431
		Forensic Medicine (Smith and other)	183	Physiology, Human, Principles of (Starling) (Evans)	33
		— Medicine and Toxicology, Aids to (Robertson)	229	— Recent Advances in (Newton)	282
		Geriatric Medicine (Stieglitz)	530	— A Textbook of (Fulton)	229
		Gynaecology, Diagnostic, Handbook of Obstetrics and (Doyle)	430	Psychosomatic Diagnosis and Treatment, Synopsis of (Dunbar <i>et al.</i>)	81
		— Obstetrics and, A Synopsis of (Bourne)	32	Radiotherapy and Cancer (Taylor <i>et al.</i>)	81
		Happy Toil: Fifty-five Years of Tropical Medicine (Rogers)	430	— A Short Textbook of (Walter and other)	529
		Health Service, The National (Hill and other)	131	Rat in Laboratory Investigation (Farris and other)	283
		Heart and Circulation, A History of the (Willius and other)	131	Refraction, The Practice of (Duke-Elder)	132
		Histology, Textbook of (Maximow and other)	331	Reproduction, Sex and, Disorders of (Pillay)	482
		Hygiene (Currie and other)	228	Rheumatic Diseases (Kersley)	528
		Laboratory Investigation, The Rat in (Farris and other)	282	Sex Endocrinology, Female (Birnborg)	228
		— Methods and Diagnosis, Clinical (Gradwohl)	82	— and its Mysteries (Scott)	183
				— and Reproduction, Disorders of (Pillay)	482

	Page		Page		Page	
Skin, Common Diseases of the (Low and other) ..	429	Rohini, D. K., <i>see</i> Abdulla, M. Chemotherapy of Cholera with a New Sulphone Compound (O. A.) ..	202	Sclerema Neonatorum, Report of a Case of (Shadaksharappa) (M. H. P.) ..	556	
— Diseases in General Practice (Bettley) ..	32	Rose, H. M., and other. Aureomycin in the Treatment of Infectious Diseases (C. T.) ..	476	Scott, G. R. Sex and its Mysteries ..	183	
Social Medicine, Recent Advances in (Stevenson) ..	582	Ross, R. A Garbled Quotation from Institute of Tropical Hygiene: Course in Tropical Hygiene (Ponsford) (M. N.) ..	263	Scrotum, An Unusual Case of Lymphocele of the (Tribedi) (M. H. P.) ..	256	
Statistics, Medical, Principles of (Hill) ..	283	Routh, J. I. Fundamentals of Inorganic, Organic and Biological Chemistry ..	379	Scrub-Typhus, Chloromycetin in (Giles and other) (C. T.) ..	274	
Surgery, Basic (Sen) ..	131	Roy, A. C., <i>et al.</i> Studies in Antimalarials (M. N.) ..	512	— Fever with Unusual Neurological Signs, Brief Notes on Two Cases of (Rao) (M. H. P.) ..	103	
— General, Operations of (Orr) ..	131	— A. R., <i>see</i> Tribedi, B. P. Malformations of the Fetus (O. A.) ..	144	— Laboratory Diagnosis of (Swamy) (O. A.) ..	297	
— A Textbook of by American Authors (Christopher) ..	131	— D. M. Note on Diet Surveys Carried out in the Central Provinces and Berar (P. H. S.) ..	320	Sen, A. K. Basic Surgery ..	131	
Syphilis (Thomas) ..	379	— I. B. Typhus in Myllem State Area, Shillong (O. A.) ..	99	— N. C. Vaginal Cyst (M. H. P.) ..	455	
Teaching, Clinical, Ward Administration and (Gipe and other) ..	131	Rozansky, R., and other. Excretion of Penicillin in Human Milk (C. T.) ..	31	— P. C. A Case of Accidental Paludrine Poisoning (M. H. P.) ..	305	
Toxicology, Forensic Medicine and, Aids to (Robertson) ..	229	Rudra, M. N., and Kant, L. A Field Investigation into Lathyrism (P. H. S.) ..	415	— P. C. Two Cases of Vesicular (Weeping) Eczema Treated with Antihistaminic Drug (M. H. P.) ..	54	
Tropical Medicine, Fifty-five Years of: Happy Toil (Rogers) ..	430			Seneca, H., <i>et al.</i> Synergistic Action of Penicillin and Streptomycin on <i>Endameba histolytica</i> Cultures (C. T.) ..	125	
— Therapeutics, A Treatise on (Chopra <i>et al.</i>) ..	528			Sen Gupta, A., and Mitra, S. K. An Observation on Preserved Ova of <i>Ascaris Lumbricoides</i> (O. A.) ..	138	
Tuberculosis (Pottenger) ..	379			— P. C. Hydroxystilbamidine in the Treatment of Indian Kala-Azar (O. A.) ..	547	
— Index and Abstracts of Current Literature (National Association for the Prevention of Tuberculosis) ..	130			— P. C. Treatment of Kala-Azar with Methyl Glucamine Antimoniate (O. A.) ..	291	
— Pulmonary, Artificial Pneumothorax in (Heaton) ..	379			— P. C., Basu Mallick, K. C., and Bhattacharya, B. A Rapid Method of Iron Hamatoxylin Stain for Protozoa in Tissue Sections and Smears (O. A.) ..	400	
Vision, Recent Advances in the Physiology of (Hartridge) ..	582			— P. C., <i>see</i> Chakravarti, R. N. Urinary Excretion of Antimony after Administration of Methyl Glucamine Antimoniate (O. A.) ..	388	
Vitamin A Requirement of Human Adults (M.R.C. Special Report Series No. 264), 1949 (Med. Res. Council) ..	331			— P. C., <i>see</i> Gupta, J. C. Aurcomycin in Kala-Azar (C.) ..	384	
Ward Administration and Clinical Teaching (Gipe and other) ..	131			— P. C., Panja, D., and Banerjee, A. K. An Unusual Case of Post-Kala-Azar Dermal Leishmaniasis (O. A.) ..	138	
Waters and Water Supplies, The Examination of (Taylor) ..	529			Serological Technique: Immunotherapy (<i>contd.</i>) (Grevil) (O. A.) ..	453	
Women, Diseases of, By Ten Teachers (White <i>et al.</i>) ..	32			— Technique: Immunotherapy (<i>contd.</i>) (Grevil) (O. A.) ..	554	
Wounds, Industrial, of the Hand, Infection and Sepsis in (Williams and Miles) ..	582			Service Notes 84, 134, 233, 334, 483 ..	483	
Rh Factor, Post-Necrotic Scarring of the Liver in a Child and its Possible Relationship to (Tribedi and Chanda) (O. A.) ..	192			Settling Tanks in Two Water Purification Plants in India, Efficiency of (Subrahmanyam and Majumder) (P. H. S.) ..	565	
Rheumatism, Cortisone in the Treatment of (C. T.) ..	124			Sex Hormones, Studies on, Part I (Mohanty and Pabrai) (O. A.) ..	43	
Rice, C. O., <i>et al.</i> Parenteral Nutrition in the Surgical Patient as Provided from Glucose, Amino Acids and Alcohol (C. T.) ..	520			Sexual Disorder in 'Mepacrine Psychoses' (Kapur and Das Gupta) (M. H. P.) ..	20	
Rindani, T. H., and Rao, S. N. N. Studies of the Urinary Excretion of Nicotinic Acid in Diabetic Patients (O. A.) ..	488			Shadaksharappa, K. S. Report of a Case of Sclerema Neonatorum (M. H. P.) ..	556	
Rinzler, S. H. Re-Emphasis of the Auscultatory Method for Ascertaining the Size of the Liver (C. T.) ..	577			Shah, M. J. Chloramphenicol in Typhoid Fevers (C. T.) ..	526	
Robertis, E. D. P. de, <i>et al.</i> General Cytology ..	228			Shaw, W. A Textbook of Midwifery ..	130	
Robertson, W. G. A. Aids to Forensic Medicine and Toxicology ..	229					
Robinson, J. M. Procaine Penicillin with Aluminum Monostearate (C. T.) ..	224					
Rock Salt Deposits of Mandi (M. N.) ..	213					
Roentgen Rays in the Treatment of Cutaneous Diseases (Lane) (C. T.) ..	580					
Rogers, K. B., and others. Chloramphenicol in Treatment of Infantile Gastro-Enteritis (C. T.) ..	272					
— L. Happy Toil: Fifty Years of Tropical Medicine ..	430					

	Page		Page		Page
Shoplifting, An Unusual Case of (C. T.) ..	274	Streptomycin, Para-Aminosalicylic Acid and, Treatment of Pulmonary Tuberculosis with (C. T.) ..	272	Sulphonates in the Treatment of Leprosy, The Present Status of (Dharmendra) (Erratum) ..	456
Shortt, H. E. (M. N.) ..	316	Penicillin and, on <i>Endamaba histolytica</i> Cultures, Synergistic Action of (Seneca <i>et al.</i>) (C. T.) ..	125	Sulphur, Cultivating Germs to Produce (Goldsmith) (M. N.) ..	510
Shroff, B. S. Memorial Gold Medal of the Bombay Medical Union (M. N.) ..	28	and Sulphadiazine, An Outbreak of Plague in an Epidemic Form Treated with (Ghosh) (O. A.) ..	441	Sunderman, F. W., and other, <i>Normal Values in Clinical Medicine</i> ..	283
Silver, M. Y. Problem of Weakness and Fatigue (C. T.) ..	31	in Syphilis (Gokhale and Ranade) (O. A.) ..	253	Swamy, T. V. Laboratory Diagnosis of Scrub Typhus (O. A.) ..	297
Simonton, K. M. Streptomycin Treatment of Ozena (C. T.) ..	281	in Tick-Borne Relapsing Fever of Kashmir (Narain and Kalra) (O. A.) ..	87	T. V. Wassermann Reaction (C.) ..	84
Singh, B., <i>see</i> Das, N. Iliacus Minor (O. A.) ..	492	Treatment of Infantile Diarrhoea and Vomiting (Holzel <i>et al.</i>) (C. T.) ..	223	Syphilis, Control of (M. N.) ..	366
—B., and Khanna, H. Muscular Anomalies (O. A.) ..	391	Treatment of Ozena (Simonton) (C. T.) ..	281	Curable with a Single Penicillin Treatment? (M. N.) ..	559
—K. Intensified Electrical Convulsive Therapy in a Military Hospital (O. A.) ..	41	The Use of (M. N.) ..	263	Seminars, International, W.H.O. to Sponsor (M. N.) ..	361
—K. Pulmonary Moniliasis (O. A.) ..	10	Subdeltoid Bursitis (Wylie) (C. T.) ..	179	Streptomycin in (Gokhale and Ranade) (O. A.) ..	253
—T. Treatment of Infantile Cirrhosis of the Liver (C.) ..	531	Subrahmanyam, K., and Bhaskaran, T. R. The Risk of Pollution of Ground Water from Borehole Latrines (P. H. S.) ..	418		
Slocum, D. B. <i>An Atlas of Amputations</i> ..	131	K., and Majumder, N. Efficiency of Settling Tanks in Two Water Purification Plants in India (P. H. S.) ..	565	T	
Smadel, J. E., <i>et al.</i> Relation of Relapses in Typhoid to Duration of Chloramphenicol Therapy (C. T.) ..	220	P., <i>see</i> Sanghvi, L. M. Acute Gastro-Enteritis due to <i>B. vincenti</i> and <i>B. fusiformis</i> (O. A.) ..	437	Talbot, D. R., <i>et al.</i> Epilepsy as a Sequela of Recurrent Malaria (C. T.) ..	277
—J. F. Clinical Use of the Antibiotic Chloramphenicol (Chloromycetin) (C. T.) ..	523	Sulpha and Sulphone Drugs (Basu) (C.) ..	534	—D. R., <i>et al.</i> Epilepsy as a Sequela of Recurrent Malaria (C. T.) ..	428
Smallpox, Incidence of Arthritis in (Chatterjee) (O. A.) ..	49	Sulphadiazine, Penicillin and, in Lobar Pneumonia (Chatterjee) (C.) ..	233	Tandon, H. C. D., <i>see</i> Wahi, P. N. Primary Systemic Amyloidosis (O. A.) ..	537
—India Aids Burma to Fight (M. N.) ..	112	Streptomycin and, An Outbreak of Plague in an Epidemic Form Treated with (Ghosh) (O. A.) ..	441	Tassman, I. S. <i>The Eye Manifestations of Internal Diseases</i> ..	331
—Vaccine (M. N.) ..	409	and Sulphaguanidine in the Treatment of Acute Bacillary Dysentery, Comparative Value of (Khan) (O. A.) ..	490	Taylor, A. G. C., <i>et al.</i> <i>Radiotherapy and Cancer</i> ..	81
Smith, E., <i>et al.</i> Management of the Symptom Complex in Acute Poliomyelitis (C. T.) ..	375	Sulphaguanidine, Sulphadiazine and, in the Treatment of Acute Bacillary Dysentery, Comparative Value of (Khan) (O. A.) ..	490	—E. W. <i>The Examination of Waters and Water Supplies</i> ..	529
—S., and other. <i>Forensic Medicine</i> ..	183	Sulphonamides and Sulphonates (E.) ..	506	—H. E., and other. <i>The Cytological Diagnosis of Malignant Cells in Various Body Fluids</i> (C. T.) ..	182
Snake Farm, Brazil's (Pastore) (M. N.) ..	361	Sulphone Compound, A New, Chemotherapy of Cholera with (Abdulla and Rohini) (O. A.) ..	202	Terias <i>hecabe</i> Linnaeus, New Antibiotic for Malaria, Extract of Wings of Philippine Butterfly (Garcia) (C. T.) ..	423
Snyder, F. F. <i>Obstetric Analgesia and Anesthesia</i> ..	282	Group in Leprosy, Experimental Work with (C. T.) ..	370	Thakkar, K. V. Unusual Cure of Angina Pectoris after Virus Disease (C.) ..	84
Soapless 'Soap' (M. N.) ..	212	Sulphones, Sulphonamides and (E.) ..	506	Thakurta, P. C., <i>see</i> Datta, S. K. Effect of Fibrolysin and Anti-Thyroidin on Raynaud's Disease after Sympathectomy (M. H. P.) ..	102
Sodium Propionate in the Treatment of Pruritus Vulvæ (C. T.) ..	427	Thromboangiitis Obliterans, Follow-Up Study of Patients with (Campbell <i>et al.</i>) (C. T.) ..	520	Therminometers, Clinical, Sterilization of (C. T.) ..	330
Solaniki, K. G. A Case of Hydro-nephrotic Kidney (M. H. P.) ..	402	Thyrototoxicosis, The Present Status of the Treatment of (Beirwaltes and other) (C. T.) ..	127	Thioarsenites in Amoebiasis (C. T.) ..	373
Soman, D. W. The Incidence and Distribution of Murine Typhus amongst Bombay Rats (O. A.) ..	249	Tidy, H. <i>Edited by—The Medical Annual, 1950</i> ..	581	—in Amoebiasis (Anderson <i>et al.</i>) (C. T.) ..	221
—K. S. Treatment of Threadworms and of Stammering (A. Q.) ..	333			Thomas, E. W. <i>Syphilis: Its Course and Management</i> ..	379
Spicknall, C. G., <i>et al.</i> The Treatment of Falciparum Malaria with Intramuscular Chloroquine (C. T.) ..	476			—T., and Kamath, M. V. Oral Novocaine Therapy in Peptic Ulcer (O. A.) ..	16
Sprague, R. G., <i>et al.</i> Observations on the Physiologic Effects of Cortisone and ACTH in Man (C. T.) ..	522			Thompson, H. L., and other. <i>Melena</i> (C. T.) ..	369
Squibb-Sarabhai Chemicals Collaboration (M. N.) ..	563			Thoracoplasty, Contra-Lateral Fracture of the First Rib following (Dingley) (O. A.) ..	14
Stammering, Threadworms and, Treatment of (Soman) (A. Q.) ..	333			Threadworm Ova, An Improved Swab for the Detection of (C. T.) ..	282
Standards (Draft) for Sulphuric, and Boric ..	263			Threadworms and Stammering, Treatment of (Soman) (A. Q.) ..	333
—, and (C.) ..	576			—Treatment of (Dathathuri) (A. Q.) ..	434
Steigmann, <i>et al.</i> Flocculation Tests in the Diagnosis of Hepato-Biliary Disease (C. T.) ..	224			Thromboangiitis Obliterans, Follow-Up Study of Patients with (Campbell <i>et al.</i>) (C. T.) ..	520
Steinberg, N. Continuous Antibiotic Therapy (C. T.) ..	478			Thyrototoxicosis, The Present Status of the Treatment of (Beirwaltes and other) (C. T.) ..	127
Sterile Washing-Up (C. T.) ..	576			Tidy, H. <i>Edited by—The Medical Annual, 1950</i> ..	581
Stevenson, A. C. <i>Recent Advances in Social Medicine</i> ..	582				
Stieglitz, E. J. <i>Edited by—Geriatric Medicine</i> ..	530				
Streptomycin in Biliary Tract Infection (Chaudhuri and Chakravarti) (M. H. P.) ..	555				

Page	Page	Page
Tingling, Acute, A Case of (Ghose) (M. H. P.) .. 257	Typhoid Vaccine in Treatment of Certain Ophthalmic Diseases (Curry and other) (C. T.) .. 224	Vitamin B ₁₂ Therapy, Failure of, in Pernicious Anemia of Pregnancy (Furman et al.) (C. T.) .. 576
Tonsillectomy, Poliomyelitis and (C. T.) .. 222	—Vaccine in Treatment of Certain Ophthalmic Diseases, Continuous Intravenous Injection of (Curry and other) (C. T.) .. 121	—E (C. T.) .. 575
Toothache, Relief of (C. T.) .. 426	Typhus, Cystitis, Pertussis, Typhoid, Aureomycin in the Treatment of (Krishnan et al.) (O. A.) .. 202	Vitamins, Parenteral Use of (Treu) (C.) .. 482
Traquair, H. M. <i>Clinical Perimetry</i> .. 132	—Murine, amongst Bombay Rats, The Incidence and Distribution of (Soman) (O. A.) .. 249	
Travel Sickness (C. T.) .. 30	—in Mylhem State Area, Shillong (Roy) (O. A.) .. 99	W
Treponematoses, The (E.) .. 506	—in the Northern Circars (Rao) (C.) .. 33	W.H.O. Antibiotics Programme (M. N.) .. 268
Treu, R. Chloromycetin in Typhoid and Para-Typhoid Fever (O. A.) .. 154	—Vaccine for Afghanistan (M. N.) .. 409	—Establishes Regional Office for Africa (M. N.) .. 558
—R. Parenteral Use of Vitamins (C.) .. 482	—Vaccine to Afghanistan, Pan-American Sanitary Bureau Sends (M. N.) .. 361	—Executive Board, Fifth Session of (M. N.) .. 118
Tribedi, B. P. An Unusual Case of Lymphocele of the Scrotum (M. H. P.) .. 256		—Executive Meets in Geneva (M. N.) .. 71
—B. P., and Chanda, N. K. Post-Necrotic Scarring of the Liver in a Child and its Possible Relationship to Rh Factor (O. A.) .. 192	U	—Experts on Drug Addiction Meet to Advise U.N. (M. N.) .. 72
—B. P., and Dutta Gupta, A. K. Tumours of Endothelial Origin (O. A.) .. 239	Undecylenic Acid in Psoriasis, Peroral Administration of (Perlman and other) (C. T.) .. 125	—in the Field (M. N.) .. 117
—B. P., and Roy, A. R. Malformations of the Fetus (O. A.) .. 144	Uranium Poisoning, BAL and (C. T.) .. 280	—First Deputy Director-General of, Appointed (M. N.) .. 461
Tropical Medicine and Hygiene, Bengal, Faculty of (L.T.M. Examination Results), 1950 (M. N.) .. 512	Urinary Tract, Infections of the, Aureomycin in (Franklin) (C. T.) .. 179	—and the Government of Ceylon, Signing of an Agreement Between (M. N.) .. 111
Tuberculosis, Against Pessimism in (E.) .. 261	Utrecht, Fair, 1950 (Graafland) (M. N.) .. 367	—Regional Committee for South-East Asia, Third Session of (M. N.) .. 507
—Conference to be held in Hyderabad (M. N.) .. 560	V	Wagle, M. S. Uterine Manifestations of Vitamin-B Deficiency (M. H. P.) .. 404
—Histoplasmosis and (C. T.) .. 378	Vaccine Lymph, Efficacy of Penicillin in Reducing Bacterial Contamination in (Das Gupta) (P. H. S.) .. 514	Wahi, A. L. A Case of Sciatica due to Malaria (M. H. P.) .. 255
—in India .. 271	Vaccinia Virus and its Neutralization by Penicillin, Toxic Factor(s) in (Murthy) (O. A.) .. 487	—P. N., and Samuel, K. C. The Place of Clinical Pathological Museum in Medical Education (O. N.) .. 54
—Problem in India (M. N.) .. 407	Vaginal Cyst (Sen) (M. H. P.) .. 455	—P. N., and Tandon, H. C. D. Primary Systemic Amyloidosis (O. A.) .. 537
—Pulmonary, Para-Aminosalicylic Acid (P.A.S.) in (Nagley and other) (C. T.) .. 79	Vagotomy for Peptic Ulcer, Early and Delayed Clinical Effects of (Kipen and other) (C. T.) .. 427	Waisbren, B. A., and other. Aureomycin and Aluminum Hydroxide (C. T.) .. 276
—Pulmonary, Para-Aminosalicylic Acid and Streptomycin, Treatment of (C. T.) .. 272	Valves, New Sub-Miniature (M. N.) .. 117	Walter, J., and other. <i>A Short Textbook of Radiotherapy</i> .. 529
—Seals Sale (M. N.) .. 408	Varmali, K., sec Reddy, D. G. <i>Paraphostomum sufaritayex</i> (Intestinal Fluke) Infection in Man (O. A.) .. 546	Wassermann Reaction (Swamy) (C.) .. 84
—Turkey to Intensify Fight against (M. N.) .. 112	Vasudevamurthy, B. Treatment of Infantile Cirrhosis of the Liver (C.) .. 532	Water Hyacinth, Control of (M. N.) .. 560
Tuckman, E. Rural Health Problems in China (C. T.) .. 574	Vaughan, W. T. <i>Practice of Allergy</i> .. 227	—Purification Plants in India, Efficiency of Settling Tanks in Two (Subrahmanyan and Majumder) (P. H. S.) .. 565
Tumours of Endothelial Origin (Tribedi and Dutta Gupta) (O. A.) .. 239	Vay, D. L., and other. Deoxycortone Acetate and Ascorbic Acid in the Treatment of Rheumatoid Arthritis (C. T.) .. 274	Weakness and Fatigue, The Problem of (Silver) (C. T.) .. 31
Typescript, Etc., Preparing a (E.) .. 308	Vegetable Drugs, Australia Looks for (M. N.) .. 465	Weight-Reducing Diet, A Simple (Marriott) (C. T.) .. 123
Typhoid Fever with Bacteriophage, Treatment of (Biswas) (C.) .. 583	Venereal Disease Programme of the W.H.O. (Cutler) (O. N.) .. 22	Weiss, E., and other. <i>Psychosomatic Medicine</i> .. 228
—Fever with Bacteriophage, Treatment of (Dhayagude and other) (C. T.) .. 423	—Disease, Recent Advances in the Study of (Moore) (C. T.) .. 425	White, C., et al. <i>Diseases of Women by Ten Teachers</i> .. 32
—Fever, Protracted Nervous Complications of (Jennings) (C. T.) .. 275	Viswanathan, D. K. A Study of the Effects of Malaria Control Measures on Population and Vital Statistics in Kanara and Dharwar Districts (C. T.) .. 376	Williams, T. I. New Uses for Plastics (M. N.) .. 314
—Fever after Treatment with Chloramphenicol, Relapse in (Briggs) (C. T.) .. 475	Vitamin B Deficiency, Uterine Manifestations of (Wagle) (M. H. P.) .. 404	—T. I. Search for New Source of Anti-Arthritic Drug (M. N.) .. 411
—Fever, Chloramphenicol in (Shah) (C. T.) .. 526	—B ₁₂ and Ascorbic Acid, An Incompatibility Between (C. T.) .. 329	—and Miles. <i>Infection and Sepsis in Industrial Wounds of the Hand</i> .. 582
—and Paratyphoid Fever, Chloromycetin in (Treu) (O. A.) .. 154		Willius, F. A., and other. <i>A History of the Heart and the Circulation</i> .. 131
—Relapses in, to Duration of Chloramphenicol Therapy (C. T.) .. 370		Wilson, G., et al. Dangers of Intrathecal Medication (C. T.) .. 125
—Relapses in, to Duration of Chloramphenicol Therapy, Relation of (Smadel et al.) (C. T.) .. 220		—G. S. The Bacteriology of Food Poisoning (C. T.) .. 127
—Typhus, Cystitis and Pertussis, Aureomycin in the Treatment of (Krishnan et al.) (O. A.) .. 202		Winckel, Ch. W. F. A Note on the Dosage of Quinine to be Administered in Acute Malaria (C. T.) .. 576

	Page		Page		Page
Winner, P. World Braille—An Advance Toward One World (C. T.) ..	327	World Health Organization, Venereal Disease Programme of the (Cutler) (O. N.) ..	22	Y	
Winsbury-White, H. P. Renal Calculus (C. T.) ..	278	———Medical Association, The (M. N.) ..	116	Yaws Campaign in Indonesia (M. N.) ..	509
Winter in Calcutta, 1949-50 (E.)	59	Wylie, P. E. Subdeltoid Bursitis (C. T.) ..	179	———Control Campaign in Thailand (M. N.) ..	463
World Braille (Winner) (C. T.)	327			———Control Project, Vast, Indonesia Launches (M. N.) ..	364
———Health Assembly, Third (M. N.) ..	268, 269			Yellow Fever, Heparin in (Ahuja and other) (C.) ..	233
———Health Assembly, Third (M. N.) ..	309	X			
———Health Organization Fellowships (M. N.) ..	108	Xeroderma Pigmentosa in a Sinhalese, A Case of (Cooray and Joseph) (M. H. P.) ..	101	Z	
				Zahorsky, J. Synopsis of Paediatrics ..	130